Maryland
STATE MEDICAL JOURNAL

Medical and Chirurgical Faculty of the State of Maryland

VOLUME 5 *May, 1956* NUMBER 5

Scientific Papers

Chemotherapy Panel

CURRENT ASPECTS OF THE CHEMOTHERAPY OF TUBERCULOSIS[1]

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In considering those aspects of antimicrobial therapy which might warrant discussion in a symposium of this nature, one may wonder at the selection of as specific a subject as "the chemotherapy of tuberculosis." I have done so, however, in view of the fact that comment concerning developments which have taken place in the field of tuberculosis in recent years may serve to illustrate certain important aspects of antimicrobial therapy in general.

Tuberculosis represents one of the few chronic infectious diseases that has been studied extensively insofar as antimicrobial effects are concerned. Many of the observations made in relation to this disease, and many of the facts established and questions raised apply equally well to other of the chronic infectious processes which thus far are but poorly controlled by the known antimicrobial agents.

In general the microorganisms responsible for the acute bacterial infections which have responded so well to penicillin and the tetracyclines are located in readily accessible areas within the host. Experience has shown that susceptibility of the invading organism to an antibiotic generally is a sufficient basis for the assumption that a therapeutic response will be achieved with that antibiotic, provided adequate dosage is used. Distribution of the drug throughout the extracellular fluids of the body, with measurable concentrations in the blood, creates a situation in which the organisms are as vulnerable to attack by the antibiotic, as they would be in an in vitro system.

The situation however insofar as the more chronic types of infectious disease are concerned differs markedly. In these, the invading microorganisms frequently are located in areas of necrosis which contain numerous factors that

[1] Presented at the One Hundred and Fifty-sixth Annual Meeting of the Medical and Chirurgical Faculty of the State of Maryland, on Tuesday afternoon, April 27, 1954, in Osler Hall, 1211 Cathedral Street, Baltimore 1, Maryland.

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may prevent an antimicrobial agent from acting against the organisms contained therein.

As you well know, tuberculosis may be acute or extremely chronic in nature. Although identified by a common pathology and by a common etiology, its symptomatology and course are modified to a marked extent by the tissue in which it occurs and its manifestations therefore are multiple. Thus tuberculosis, both an acute and a chronic disease, a generalized and a localized infection, serves well to illustrate our points today.

1. Nature of the Lesion: Any discussion of the chemotherapy of tuberculosis necessarily must include comment concerning streptomycin, viomycin, isoniazid, para aminosalicylic acid, and the other currently available antituberculous agents. Ten years have elapsed since the discovery of streptomycin and since the first demonstration that this agent could exert an antituberculous effect in vivo, as well as in vitro. Although it was little recognized in 1944–45 that the observations made during those years would have such far-reaching effects, nonetheless it was not difficult to demonstrate the usefulness of streptomycin in the treatment of the acute forms of tuberculosis, that is, in meningeal and miliary disease. Although a severe criterion of effectiveness, the difference between life and death is easily detected and measured, and the prolongation of life in patients with meningeal and miliary tuberculosis was ample evidence that the drug had some effect upon the tubercle bacillus in vivo. In pulmonary tuberculosis, however, especially when a considerable amount of tissue destruction had taken place, the situation was more complex. One could not expect that any chemotherapeutic agent could replace caseous material or fibrous tissue, with alveoli, and that a chemotherapeutic agent would be effective in the treatment of long-standing fibro-cavernous disease. The important question however was: Could a chemotherapeutic agent, such as streptomycin, be effective in the treatment of patients with relatively non-destructive exudative disease? It is not necessary to elaborate on the remarkable effects that have since been demonstrated with streptomycin, alone or in combination with other antituberculous drugs. This audience knows far better than I the remarkable effects that have been achieved, and, for our present purpose, it is sufficient to call attention to certain facts in this regard.

2. Penetration of Streptomycin into the Lesion: The varied nature of tuberculosis as a disease, with its frequent extensive tissue destruction, led to early recognition of the fact that the nature of the lesion might influence markedly the result achieved, and to recognition of the fact that distribution of the drug throughout the extracellular fluids of the body might not be sufficient. In contrast to the situation with more acute generalized infections, the inaccessibility of the organisms within the lesions made it logical to assume that penetration of the drug into the lesion would be essential. Clinical studies soon demonstrated that therapeutic results could be achieved in patients with cavitary disease and that organisms recovered from these patients often were resistant to streptomycin. This fact suggested that the drug must have been in contact with the microorganisms within the lesion, and penetration of streptomycin into tuberculous lesions was subsequently confirmed by microbiological assays on resected tissue. Actually it has not been demonstrated that streptomycin maintains its antimicrobial activity in necrotic tissue—although its presence there has been demonstrated. Indeed, it is highly likely that the pH is such that streptomycin would not be active but more precise information on this point is needed. It is of interest that certain other agents, although active against the tubercle bacillus in vitro, and although capable of being absorbed and distributed throughout the body fluids, have since been found to be either inactivated by substances within necrotic tissue, or diminished

in activity when at the pH of inflammatory tissue.

3. Penetration of Streptomycin into Monocytes: Although there is no information to date concerning the relative proportions of intra- and extra-cellular bacilli in various types of tuberculous lesions, nonetheless the fact that many of the bacilli do exist within monocytes makes it apparent that an antimicrobial agent will be fully effective only if capable of penetrating not only into the lesion but also through the cell membrane. Of special interest in this regard are the observations of Mackaness who has presented evidence to show that isoniazid is as effective intracellularly as extracellularly, that streptomycin is partially effective under intracellular conditions, and that para aminosalicylic acid is totally ineffective under such conditions. Thus it is probable that the relative activities of antituberculous compounds may be related, at least in part, to the relative ease with which they diffuse through cell membranes and to the degree of activity which they can exert in an intracellular environment.

4. Bacteriostatic vs. Bactericidal Effects: It is difficult to estimate the extent to which the intracellular location of microorganisms may interfere with drug action. In like manner it is difficult to estimate the degree of bactericidal or bacteriostatic action that may result under such conditions. In the case of tuberculous meningitis, prolongation of life due to streptomycin is sufficient to indicate that a bactericidal *or* bacteriostatic effect has occurred. However not all streptomycin-treated meningitic patients have survived, and, as early as 1946, a new disease with a symptomatology and pathology quite its own,—namely, chronic tuberculous meningitis,—was recognized. The development of this disease was accepted as evidence that only a bacteriostatic, and not a bactericidal effect, had been achieved in these individuals.

In 1951, D'Esopo and his associates reported that the tubercle bacilli in "closed" necrotic pulmonary lesions could not be cultivated in vitro by standard microbiologic technics after long-term chemotherapy with streptomycin and para aminosalicylic acid. This observation was confirmed by others and the conclusion was reached that the organisms "behaved as if they were dead."

The question was raised, however, as to whether or not the technics used were adequate to prove conclusively the non-viability of microorganisms. Dubos, Hirsch, and others already had presented evidence to suggest that certain physicochemical factors within the necrotic tuberculous lesion may suppress the metabolic processes of the residual bacilli lying therein, while available evidence suggested also that changes in the pathologic nature of the lesion, and thus in the environment of the bacteria within the lesion, or changes in environmental conditions in vitro, conceivably could reverse such suppressive effects.

Using a technic designed to neutralize certain of the inhibitory agents present in necrotic tissue and to "dilute out" other potentially toxic components, we in our laboratories, in collaboration with Drs. Auerbach, Small, and Comer of the East Orange Veterans Administration Hospital, have attempted to prove whether or not these residual bacilli are viable. Fourteen of nineteen patients studied during the past year had received from four to twelve months of chemotherapy pre-operatively and showed morphologic evidence of cavity closure. One had received eleven months of chemotherapy pre-operatively and showed evidence of an open cavity with healing. Viable tubercle bacilli were recovered from twenty of the twenty-eight lesions from these fifteen patients, or from ten of the fifteen patients. Thus it seems possible that improved cultural technics may increase the frequency with which viable tubercle bacilli may be recovered from "closed" or healed tuberculous lesions. When these data are compared, however, with the results obtained by D'Esopo and his associates, it becomes apparent

that other factors may be of importance. If sterilization of lesions can occur, either the duration of chemotherapy must exceed twelve months to achieve this effect, or daily streptomycin must be more effective than twice weekly streptomycin. Studies are currently in progress in our laboratories, in collaboration with the East Orange and West Haven Veterans Administration Hospitals, to evaluate in this respect daily versus twice weekly streptomycin, and long-term regimens in excess of twelve months.

The important point at present is the fact that, after extensive chemotherapy ranging from four to twelve months, using a regimen widely employed today (e.g., twice weekly streptomycin with daily para aminosalicylic acid), tubercle bacilli may remain viable in apparently "closed" necrotic or healed lesions, and that the viability of these organisms can be demonstrated in many instances. Undoubtedly not all of the bacilli present in these lesions are viable, any more than all bacilli in an in vitro culture are viable. Nonetheless a portion are alive, can be cultivated in vitro when appropriate technics are used, and presumably could multiply in vivo and bring about relapse under appropriate conditions.

It would appear therefore that it is seldom, if ever, possible to eradicate every single member of a particular infecting microbial population. Chemotherapy merely slows or halts multiplication of the microorganism so that the host may effectively exert its own control mechanisms. The limits of drug therapy, in a disease such as tuberculosis, are set therefore not only by the amount of necrosis or tissue destruction that has taken place before drug therapy is started, but also by the sterilizing capacity of the drug or combination of drugs used. The limits of drug therapy can be extended only by the defense mechanisms of the body and/or by surgical intervention.

The possibility that a more rapid therapeutic result might be achieved if a bactericidal effect were accomplished is an intriguing one. Thus interest has been aroused recently in the search for new agents or combinations of agents with bactericidal properties, and in the development of better methods of demonstrating the action of these agents in vivo. Of special interest in this regard are the observations of McCune, Tompsett, and McDermott who recently showed, by means of quantitative studies on the microbial populations in lung and spleen homogenates from infected drug-treated animals, that isoniazid in combination with pyrazinamide comes closer to eradicating viable tubercle bacilli from the tissues of infected animals than any other drug or combination of drugs tested to date. Of interest furthermore is the fact that pyrazinamide alone is capable of exerting only transient or short-lived effects in vivo. Yet in combination with a compound such as isoniazid, which acts by a specific mechanism, it is a powerful drug. The possibility that other such drug-combinations may prove of importance cannot be overlooked.

5. Host Resistance: The very fact that tubercle bacilli are not eradicated from the host, with present-day chemotherapeutic agents, implies that the success of chemotherapy must depend upon the ability of the patient to control the infection after the administration of the drug has been discontinued. There is no certain way to predict the degree of resistance that may be displayed by an individual person. Resolution of lesions during the primary complex is the rule, not the exception, and speedy and extensive resolution of large well-established lesions on regimens of bed rest alone has been reported occasionally, despite the fact that, with the exception of the initial infection with the tubercle bacillus, it has never been established conclusively that a significant degree of host resistance develops during the period following the appearance of progressive pulmonary disease. Chemotherapy may speed the process of healing, or may increase the frequency of success in the individual whose lesions have developed beyond the stage of the primary complex, but it does not appear to alter significantly the basic mechanism of healing.

6. General: In a discussion of this nature one must not fail to mention two specific aspects of the chemotherapy of tuberculosis which are primarily of practical importance only. Perhaps due in part to the relatively prolonged generation time of the tubercle bacillus, and perhaps due in part to the chronic nature of the disease, the intermittent administration of streptomycin has proved adequate in most instances. The possibility thus exists that other antimicrobial agents may be effective in certain types of infection, when used on an intermittent basis. In view of the fact that not all antimicrobial agents act through the same mechanism and in view of the fact that some act only on actively dividing cells while others act also on resting cells, no generalization can be made, however, concerning the efficacy of intermittent regimens with other antimicrobial agents or other infectious processes. Experience has indicated furthermore that the pharmacologic nature of a drug influences strongly the manner in which it must be administered, if it is to be maximally effective.

Emergence of drug-resistant microorganisms, after prolonged contact with an antimicrobial, was first emphasized in relation to the sulfonamides in the treatment of gonorrhea. The phenomenon has been of great importance in relation to tuberculosis, however, and the potentialities of combinations of drugs for control of this phenomenon have been well demonstrated by investigators in this field. Already the use of combinations of agents in the treatment of other infections is becoming widespread. It is unfortunate that our knowledge of the mode of action of these agents is not yet such that one can intelligently select the best drug combination for any given purpose.

One may ask where these many observations in the field of tuberculosis have led us. Essentially they have led us to a fuller understanding of the importance of the host-parasite and drug-parasite relationships insofar as chemotherapy is concerned. Although drug-susceptibility on the part of the invading microorganism undoubtedly is an essential prerequisite to effective drug therapy, it is not a sufficient prerequisite. Knowledge of the generation time, growth requirements, and metabolic activities of the invading microorganism, knowledge concerning the type of lesion and/or tissue cell in which it resides, and knowledge of the pharmacologic properties of the drug involved,—all these are essential if one is to achieve maximal chemotherapeutic effects. This situation is not unique to tuberculosis. Tuberculosis is not the only infection in which the organisms are found in necrotic areas, nor is it the only disease in which they may be located intracellularly. Whether one is speaking of the granulomatous type of lesion present in this disease, in leprosy, and in fungous infections,—or of staphylococcal or amebic abscesses,—walled-off lesions in the substance of or on the surface of a heart valve as seen in subacute bacterial endocarditis, —or infections of the lung due to K. pneumoniae in which tissue destruction and abscess formation exist,—the ultimate results achieved with antimicrobial therapy of necessity must depend upon (1) the nature of the lesion at the start of chemotherapy, (2) the extent to which the drug can penetrate into the lesion and, if necessary, into the cell, (3) the degree of bacteriostatic or bactericidal action that the drug can exert upon the microbe at the site of infection, and lastly (4) the resistance of the host.

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THE MECHANISM OF ACTION OF CHEMOTHERAPEUTIC AGENTS[1]

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A considerable number of papers have appeared which bear either directly or indirectly on not only the mechanism of action of chemotherapeutic agents, but also on the mechanism of development of resistance to these agents. In view of this and the time limitations the following discussion will be confined to a consideration of the mechanism of action of sulfonamides, penicillin and streptomycin together with mechanisms by which the microorganism may circumvent the action of these drugs.

First, let us consider some basic facts which underlie the metabolic mechanisms that are to be presented.

During the growth of a bacterial population in a liquid medium the total number of cells increases steadily. On the other hand the number of "viable" cells, those cells having the ability to reproduce, soon reaches a maximum which is maintained as long as cell division persists.

When the total number of cells becomes steadily greater than the number of "viable" cells, population pressure acts as a selection pressure permitting the establishment of mutants with a positive selection value.[1]

In Fig. 1, this information is summarized diagrammatically. The medium contains no added known inhibitor of cell division. At 0 hours incubation time the population principally consists of parent drug sensitive (S) cells with a few drug resistant (R) cells which originated through a previous mutation. In the beginning both (S) and (R) cells reproduce, increasing the magnitude of their respective clones. However, with the onset of selection pressure the more "viable" (S) cells, having a greater positive selection value, overgrow and replace the resistant (R) mutant. In this case the metabolism of the population will be that of the (S) cells and drug sensitive. In contrast, if a known inhibitor of cell division is added to the medium then the (R) cells which are resistant to the drug will have a greater positive selection value and thus be able to replace the drug sensitive (S) cells. The curves for the (R) cells and (S) cells would then be reversed. The metabolism of the population would be that of the (R) cells and drug resistant.

In summary then it can be said that the interaction between the genitically controlled metabolic potentialities and the physiological environment determines the type of population and metabolism to be manifested. With this in mind we can now consider our primary interest—mechanisms of action of chemotherapeutic drugs and mechanisms of resistance to these drugs.

SULFONAMIDES

Fig. 2 is taken from a paper by Lampen and Jones[2] and summarizes one concept of the mechanism of action of sulfonamides.

Lockwood[3] in 1938 reported peptone as a sulfonamide antagonist. Stamp[4] in 1939, and Green[5] and Woods[6] independently in 1940 reported on sulfonamide antagonists isolated from either bacterial cells or cell-free culture fluid. Woods isolated and characterized his antagonist as an amino derivative of an aromatic carboxylic acid. On the basis of this observation and because of its structural similarity to sulfanilamide, Woods postulated p-aminobenzoic acid (PABA) as an essential metabolite which competed with sulfonamide for a common enzyme site.

Rubbo and Gillespie[7] in 1940 isolated PABA

[1] Presented at the One Hundred and Fifty-sixth Annual Meeting of the Medical and Chirurgical Faculty of the State of Maryland, on Tuesday afternoon, April 27, 1954, in Osler Hall, 1211 Cathedral Street, Baltimore 1, Maryland.

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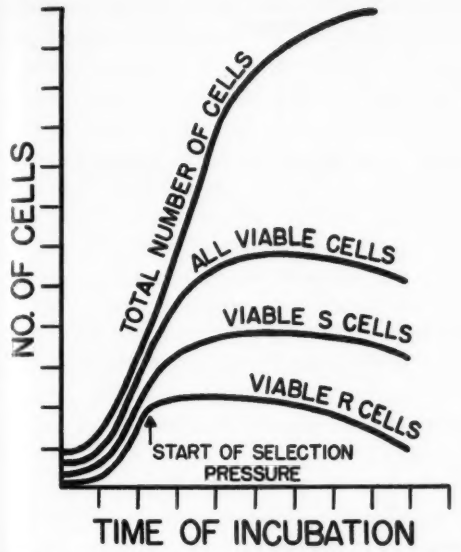


FIG. 1. The effect of selection pressure on the constitution of a bacterial population.

from yeast extracts. Ratner, et al.[8]; in 1944 demonstrated that PABA existed in a bound form as a glutamic acid peptide. Finally, Angier, et al.[9], in 1946 elucidated the structure of folic acid.

Kohn and Harris[10] and Bliss and Long[11] in 1941 reported methionine as an amino acid required for the growth of a sulfonamide resistant strain of *Escherichia coli*. Lampen, et al.,[12] reported in 1946 that methionine, purines and thymine would replace the PABA requirement for a PABA-requiring mutant and in a medium supplemented with these substrates both the parent strain and the requiring mutant were resistant to sulfonamides.

In 1945 Stetten and Fox[13] observed that during sulfonamide bacteriostasis of *Escherichia coli* a non-acetylable diazotizable amine accumulated in the media. The amine was isolated and characterized by Shive and Co-workers in 1947 as 4-amino-5-imidazole carboxamide ("Shive Compound").[14] These workers reported that glycine stimulated its production and also suggested that the amine functioned as a purine precursor.

Buchanan and his group[15] using isotopically labeled substrates have demonstrated that glycine and formate are elementary precursors of the purine molecule. Furthermore that "Shive Compound" as the ribotide is converted to inosinic acid, the ribotide of the purine hypoxanthine which has been suggested to be an intermediate in purine metabolism. Citrovorum factor, a derivative of folic acid, is thought to be the C_1 carrier in this reaction. The sources of the C_1 are formate, serine, methionine and glycine.

In summary according to this viewpoint sulfonamides block the conversion of PABA to a biologically active folic acid-like compound. The function of this latter compound is to mediate the metabolism of amino acids, purines and the pyrimidine thymine.

PENICILLIN

A variety of good experimental work has appeared in connection with the mechanism of action of penicillin. However, we shall focus our attention on the work of Gale.[16] Penicillin acts primarily upon Gram positive bacteria which characteristically possess a high concentration of magnesium ribonucleotide in their peripheral layers. This nucleotide is responsible for the specificity of the Gram stain. Gale noted that certain Gram positive microorganisms in contrast to Gram negative are able to "assimilate" or take up from their external environment amino acids which they can concentrate within themselves. Glutamic acid (and certain other amino acids) enter the cell not by a simple process of diffusion, but by an active process, enzymatically catalyzed, which requires energy supplied by exergonic metabolism such as glycolysis.

Fig. 3 summarizes diagrammatically Gale's findings. The triphenylmethane dye, crystal violet, blocks the intracellular free glutamic acid from entering the metabolic pool, while according to Gale sulfathiazole blocks its incorporation into cellular protein. Under these conditions the cell in the presence of a reasonable concentration

Possible Relations of p-Aminobenzoic Acid and Related Compounds in Bacterial Metabolism

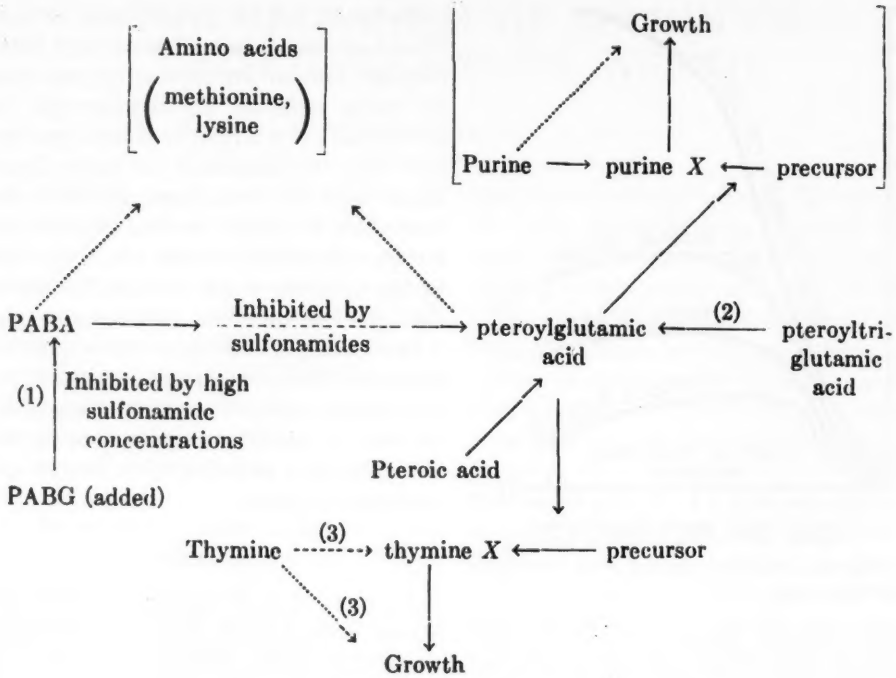
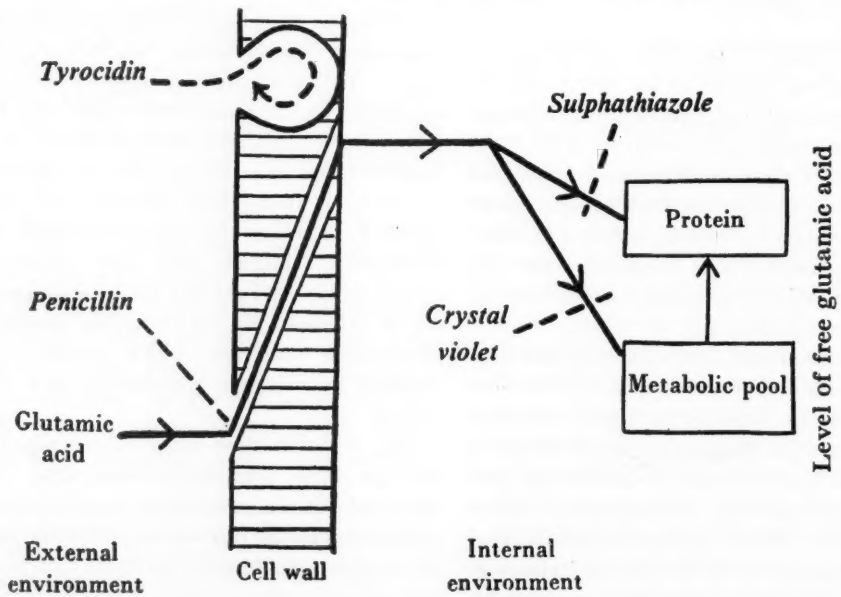


FIG. 2. From Lampen and Jones, J. Biol. Chem., **170,** 133 (1947).



Assimilation of glutamic acid by Gram-positive bacterial cell and action thereon of chemotherapeutic agents.

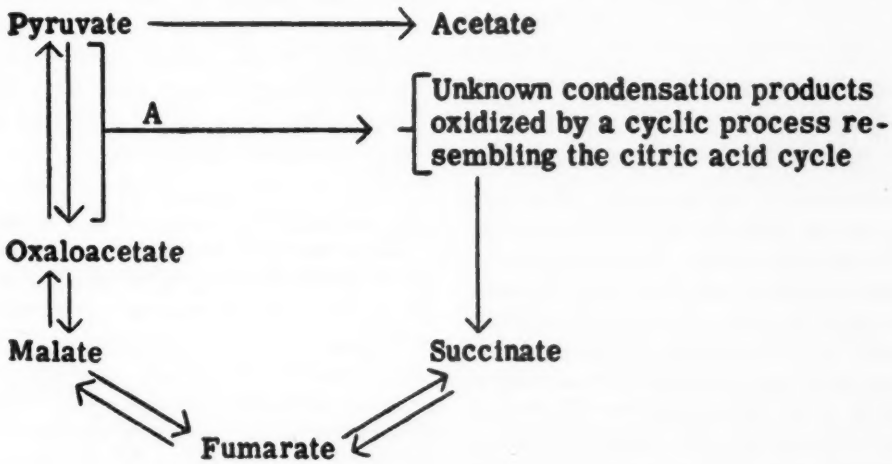
FIG. 3. From Gale, J. Gen. Microbiol., **3,** 327 (1947).

of glutamic acid in its external environment will take up and concentrate free glutamic acid internally if a source of energy such as glucose, arginine phosphate or adenosine triphosphate is present. Gale was able to show that penicillin interfered with or blocked the transport of the amino acid across the cell wall of those cells which had been cultured for a brief time in its presence. However, penicillin did not interfere with the utilization of the intracellular amino acid. In keeping with this observation on penicillin action Gale was able to demonstrate that with increase in resistance to penicillin the cells showed a decreased ability to "assimilate" the amino acid and finally not only lost this property, but also became Gram negative. Furthermore, the resistant cells were able to grow in an ammonium-salt-glucose medium requiring only thiamin, histidine and cysteine. In contrast, the sensitive cells required thiamin, niacin and a range of amino acids. Gale was able to "train" the parent sensitive strain to grow in a minimal medium such as that described for the resistant. The nutritionally inexacting strain developed in this manner was considerably more resistant to penicillin than the parent strain. Gale was also able to demonstrate an inhibition of ribose nucleic acid synthesis as demonstrated by a drop in the RNA/DNA ratio.

From the foregoing we are lead to conclude that penicillin interferes with the formation of glutamate transporting enzymes and the synthesis of RNA relative to DNA.

Streptomycin

At least three possible mechanisms of action of streptomycin have been proposed. The first reaction is that described by Cohen[17] in which the drug reacts with certain desoxyribose nucleic acids. Zeller, et al.,[18] have proposed the second mechanism of action in which the drug is reported to inhibit diamine oxidase. The third mechanism is that advanced by Umbreit and his group[19] who suggest that streptomycin acts by inhibiting terminal respiration in sensitive bacteria. Fig. 4 summarizes the viewpoint of this group which is that streptomycin inhibits the entrance of various compounds into the terminal respiration by specifically blocking oxalacetate-pyruvate reaction at A rather than blocking the



Suggested terminal oxidation processes in *E. coli* [Oginsky, Smith & Umbreit (31)].

Fig. 4

formation of "active acetate." In the absence of streptomycin the condensation products are oxidized by a cyclic process which is different from the acetate-oxalacetate system of Stern and Ochoa.[20] Development of a streptomycin-resistant strain from the parent-sensitive results in a loss of the pyruvate oxalacetate reaction.

Mechanisms of Resistance to Drug Action

A microorganism may develop resistance to the toxic action of a drug by:

1. Becoming impermeable to the drug.
2. Developing a reaction to inactivate the drug.
3. Altering the sensitive enzyme(s) so that they have little or no affinity for the drug.
4. Developing an alternate metabolic pathway.

The first two possibilities are probably specialized situations which do not cover most instances of resistance and certainly not those in which a high degree of resistance is developed. Examples of such a mechanism would be that of the penicillin inactivating enzyme penicillinase first demonstrated by Abraham and Chain[21] in (1940) and the inactivation of chloramphenicol by the "chloramphenicol reductase activity" of a resistant strain of *Escherichia coli*.[22] Sevag and Gots[22a] have reported an example of an inheritability of the impairment of an enzyme protein. Pneumococci rendered resistant to atabrine showed an impaired dehydrogenase activity resulting from an alteration of the protein moiety of the flavoprotein enzyme. The findings of Bellamy and Klimek[23] and Gale and Rodwell[24] would support the viewpoint that microorganisms circumvent the toxic action of drugs by use of alternate metabolic pathways. These workers found that as the Gram positive cells became resistant to penicillin they tended to become Gram negative, lost the energy requiring glutamate transport system and depended either upon simple diffusion or internal synthesis for their amino acid requirements. In addition, their penicillin resistant organism became a strict aerobe.

TABLE 1*

Alternate Metabolic Pathways of S. aureus

Data with respect to	Growth period	Per cent change with ST[a]	
		Susceptible (1A)	Resistant (1E)
	hrs.		
Growth	16	82	−36
	24	84	−6
	40	68	0
	65	30	0
Tryptophan utilization	16	100	−97
	24	100	−77
	40	26	−66
	65	7	−57
Glucose utilization	16	−68	80
	24	−60	49
	40	−39	33
	65	−36	21

* From Sevag and Steers, Arch. Biochem., **24,** 144 (1949). ST = 50 mg.-%.

[a] Figures indicate percentage decrease unless preceded by a minus sign, in which case they are percentage increase.

Table 1 is an analysis of the effect of sulfathiazole on the kinetics of the utilization of tryptophan and glucose by *Staphylococcus aureus.* According to Sevag and Steers[25] resistance to sulfathiazole in this instance involves an alternate metabolic pathway in which the utilization of tryptophan is critical for resistance to the drug.

TABLE 2*

Effect of Aerobiosis and Anaerobiosis upon the Growth of Staphylococcus aureus *1A (Sulfonamide-susceptible) and 1E (Sulfonamide-Resistant) Growth Period 96 hr.*[a]

Strain	Aerobic growth		Anaerobic growth	
	mg. cells/10 ml.		mg. cells/10 ml.	
	Control	ST	Control	ST
1A (susceptible)	5.7	3.5	2.4	0
1E (resistant)	4.2	4.4	0.2	0.5

* From Sevag and Steers, Arch. Biochem., **24,** 144 (1949).

[a] The medium used is that described in the experimental section. 0.5% glucose and 20 γ of tryptophan have been added. The drug (ST) concentration is 50 mg.-%.

TABLE 3*

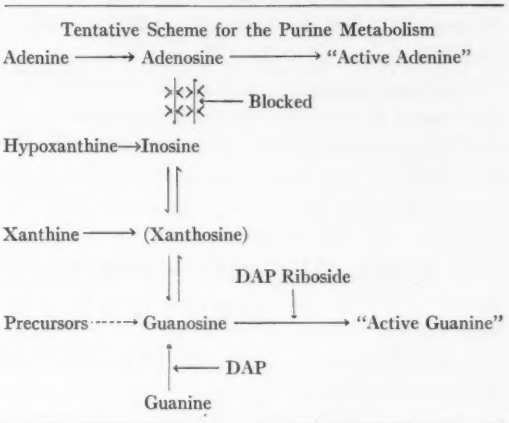
Incorporation and Synthesis of Polynucleotide Adenine and Guanine by Chloramphenicol-Sensitive and -Resistant Strains of Micrococcus pyogenes, *var.* aureus

Strain	Medium Supplemented with	PNA Purine Isolated	% From Supplement		% *de novo* Synthesis
			Ad.	Gu.	
Sensitive	adenine-8-C-14	adenine	72		
		guanine	5		95
	guanine-8-C-14	adenine		65	35
		guanine		77	
Resistant	adenine-8-C-14 guanine	adenine	107		0
		guanine	0		
	adenine	adenine		0	
	guanine-8-C-14	guanine		115	0

* From Wood and Steers, Unpublished Experiments.

TABLE 4*

The Purine Metabolism of a Chloramphenicol-Resistant Strain of Micrococcus pyogenes *var.* aureus



* From Wood and Steers, Unpublished Experiments.

Table 2 is taken from the same study and clearly shows that not only is the resistant strain a strict aerobe but also suggests that the anaerobic metabolism of the sensitive strain is sensitive to the drug whereas the aerobic metabolism is drug resistant.

Working with the same parent drug sensitive strain Wood and Steers[26] have developed from it a chloramphenicol resistant strain which has lost its ability to synthesize polynucleotide adenine and guanine from the elementary precursors and is incapable of interconverting the purine bases adenine and guanine. These findings are summarized in Table 3. Furthermore 2,6-diaminopurine (DAP) is toxic for the resistant, inhibiting the condensation of guanine and ribose whereas it is not only non-toxic for the parent strain but is incorporated to a small, but significant degree into the polynucleotide adenine and guanine. Finally, the resistant strain is a strict aerobe. Table 4 summarizes our interpretation of the chloramphenicol-resistant purine metabolism of the resistant strain. These observations can be interpreted as evidence for the interference of chloramphenicol with the nucleic acid metabolism of this strain at the elementary precursor and purine base levels. Loss of the drug sensitive sites results in chloramphenicol resistance.

In conclusion: We have seen that bacterial cells are endowed with certain genetically controlled metabolic potentialities and the interaction of the physiological environment with the available metabolic potentialities will determine whether a cell is sensitive to a chemotherapeutic agent or able to circumvent its toxic action.

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REFERENCES

1. BRAUN, W., Bact. Rev., **11,** 75 (1947).
2. LAMPEN, J. O., AND JONES, M. J., J. Biol. Chem., **170,** 133 (1947).
3. LOCKWOOD, J. S., J. Immunol., **35,** 155 (1938).
4. STAMP, T. C., Lancet **2,** 10 (1939).
5. GREEN, H. N., Brit. J. exp. Path., **21,** 38 (1940).
6. WOODS, D. D., Brit. J. exp. Path., **21,** 74 (1940).
7. RUBBO, S. D., AND GILLESPIE, J. M., Nature, **146,** 838 (1940).
8. RATNER, S., ET AL., J. Biol. Chem., **155,** 689 (1944).
9. ANGIER, R. B., ET AL., Science, **103,** 667 (1946).
10. KOHN, H. I., AND HARRIS, J. S., J. Bact., **44,** 717 (1942).
11. BLISS, E. A., AND LONG, P. H., Johns Hopk. Hosp. Bull., **69,** 14 (1941).
12. LAMPEN, J. O., ET AL., J. Biol. Chem., **164,** 789 (1946).

13. Stetten, M. R., and Fox, C. L., J. Biol. Chem., **161,** 333 (1945).
14. Shive, W., et al., J. Am. Chem. Soc., **69,** 725 (1946).
15. Buchanan, J. M., J. Cell. Comp. Physiol., **38,** 143 (1951).
16. Gale, E. F., Bull. Johns Hopk. Hosp., **83,** 169 (1948).
17. Cohen, S. S., J. Biol. Chem., **168,** 511 (1947).
18. Zeller, et al., Abstracts Am. Chem. Soc., 116th Meeting, 64G (Atlantic City, Sept., 1949).
19. Umbreit, W. W., J. Biol. Chem., **177,** 703 (1949).
20. Stern, J. R., and Ochoa, S., J. Biol. Chem., **179,** 491 (1949).
21. Abraham, E. P., and Chain, E., Nature, **146,** 837 (1940).
22. Merkel, J. R., and Steers, E., J. Bact., **66,** 389 (1953).
22a. Sevag, M. G., and Gots, J. S., J. Bact., **56,** 737 (1948).
23. Bellamy, W. D., and Klimek, J. W., J. Bact., **55,** 153 (1948).
24. Gale, E. F., and Rodwell, A. W., J. Gen. Microbiol., **3,** 127 (1949).
25. Sevag, M. G., and Steers, E., Arch. Biochem., **24,** 144 (1949).
26. Wood, R. W., and Steers, E., Unpublished experiments.

THE BROAD SPECTRUM ANTIBIOTICS WITH PARTICULAR EMPHASIS ON CHLORAMPHENICOL[1]

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The extension of the uses of antibiotics to fields other than the cure, mitigation, or treatment of diseases of man and animals may accentuate the problems already existing for the medical profession. If the use of antibiotics in animal nutrition, as crop sprays, and food preservatives becomes universal, and because of this relatively large amounts of antibiotic residues are consumed in finished foods, one might postulate not only an increase in allergic reactions, but possibly emergence of pathogenic organisms resistant to these drugs as well. Wide and sometimes unwise use of penicillin in human diseases has resulted in an increase in the number of allergic reactions and there is every reason to believe these will continue to increase. The results of a spot survey of the United States, completed in 1953, of acute anaphylactoid reactions to antibiotics is quite informative (Figure I).

Only one of the 84 penicillin reactions recorded in this survey followed administration of an oral preparation. Procaine penicillin, the most commonly used of the penicillin salts, was responsible for 55 reactions and 18 deaths. Penethamate, an hydriodide ester of penicillin used very infrequently as compared to procaine, accounted for another 26 of the 84 anaphylactoid reactions, while penicillin 'O' (allylmercaptomethyl penicillin) a penicillin which appears to have a low sensitizing potential, resulted in 2 reactions, neither of which was fatal. It is of interest that although the survey covered all anaphylactoid reactions due to antibiotics, none were found resulting from the broad spectrum drugs (chlortetracycline, oxytetracycline and chloramphenicol) and only 4 followed injection of streptomycin.

In addition to the 88 anaphylactoid reactions reported in this survey, we know of 17 others reported in the literature. With the recognition that a number of such reactions are not reported, it can be assumed we have in this country from 100 to 200 anaphylactoid reactions yearly following administration of penicillin.

There is reason to believe that the repository type of penicillin preparation may be more prone to sensitize than the soluble salts in aqueous

[1] Presented at the One Hundred and Fifty-sixth Annual Meeting of the Medical and Chirurgical Faculty of the State of Maryland, on Tuesday afternoon, April 27, 1954, in Osler Hall, 1211 Cathedral Street, Baltimore 1, Maryland.

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Type of Product	Reactions	Fatal
Procaine Penicillin (injection)	55	18
Penethamate (Diethylaminoethyl ester hydriodide) (injection)	26	5
Penicillin 'O' (Allyl mercaptomethyl penicillin) (injection)	2	0
Dibenzylethylenediamine Dipenicillin (oral tablet)	1	1
Totals	84	24

* Additional 4 reactions to streptomycin, 3 following intrathecal injection, 1 fatal; one following intramuscular injection (recovered).

FIG. I. Acute Anaphylactoid Reactions* to Penicillin

solution. With some of the insoluble salts the drug is in contact with tissue for days or even weeks. The longer period of contact of penicillin with tissue cells may result in production of partial antigens. These in turn can act as antigenic stimuli for antibody production.

In Figure II are shown the height and duration of blood concentrations of various penicillin salts.

Potassium penicillin like the sodium salt reaches a high level rather rapidly after injection and is excreted in a matter of hours. Procaine penicillin, having a lower solubility in water, is held in the tissues longer (about 24 hours) but the peak level is lower. A somewhat less soluble salt, benzylamine penicillin, acts in somewhat the same manner. The addition of a thixotropic gel of 2% aluminum monostearate in a vegetable oil to procaine penicillin further prolongs blood concentrations for up to four days but the concentration in the blood is correspondingly low. Very low concentrations of penicillin are obtained following injection of the newest of the repository penicillins, dibenzylethylenediamine dipenicillin (D B E D) but measurable amounts are observed for two weeks in some patients after an intramuscular injection of 300,000 units. Following injection of 1,200,000 units of this salt,

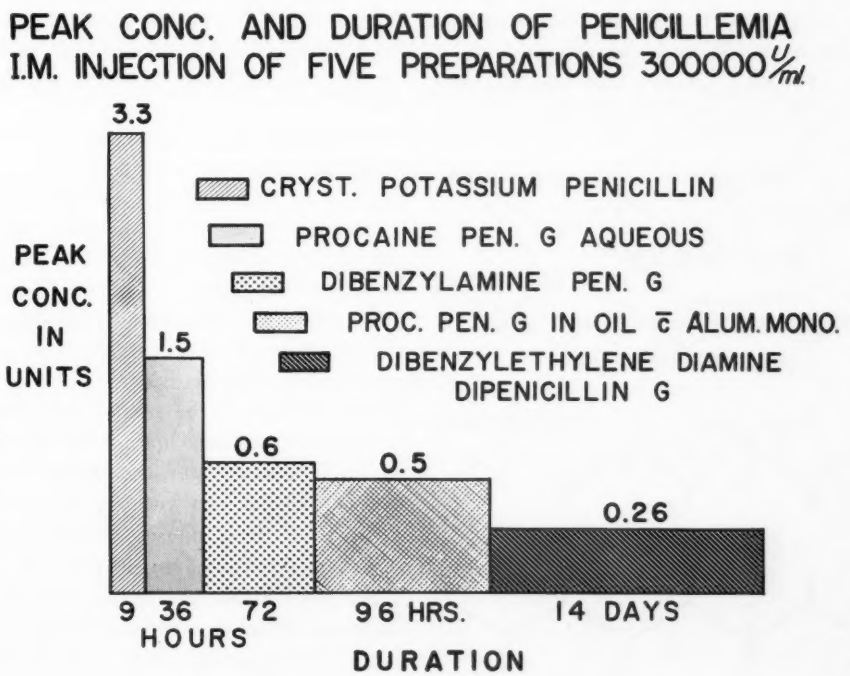


FIG. II

penicillin is found in the blood for four weeks in most patients. The repository penicillin preparations are of great value in venereal diseases and in the prophylaxis of certain infections. However, their use in asthmatics or in those individuals with a history of allergy may be dangerous.

The tetracyclines are not prone to sensitize readily. An occasional rare case of sensitivity has been reported but none of the anaphylactic type of reaction was observed in the survey referred to above. These drugs are administered in the great bulk of cases orally and this may be a factor in the low incidence of allergic reactions seen. Certainly, since tons of these drugs have been used the low sensitizing potential is not associated with lack of use.

The newest of the tetracyclines with the name "tetracycline" is a common chemical moiety of the other two, chlortetracycline and oxytetracycline. The molecular structures of all three are given in Figure III.

Tetracycline appears to be the basic molecule since it lacks an OH group at carbon 5 and a chlorine at carbon 7. Chlortetracycline, although lacking the OH group at carbon 5, has a chlorine atom at carbon 7 while oxytetracycline has the OH group at carbon 5 lacking the chlorine atom at carbon 7.

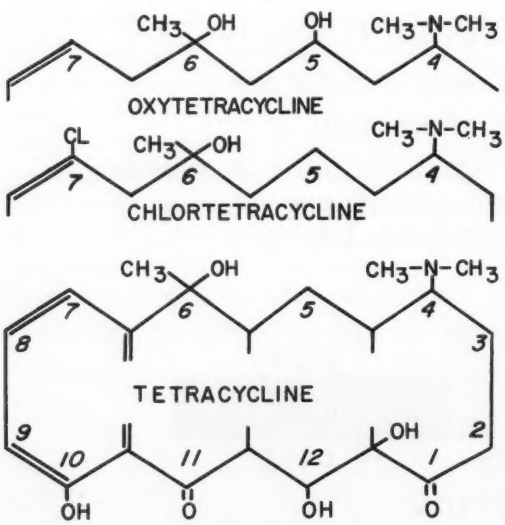


FIG. III

The tetracyclines are readily absorbed and excreted following oral administration as is the other broad spectrum drug, chloramphenicol. The dose most commonly used is 1.0 gm. daily orally and this seems adequate for most susceptible infections. In the more acute infections, 2.0 gm. daily are used. The drugs are administered intravenously only in those patients unable to take medication by mouth or in fulminating infections. Satisfactory blood concentrations are observed with all four broad spectrum drugs following doses of 0.25 gm. every 6 hours or 0.5 gm. every 6 hours (1.0 or 2.0 gm. daily) orally. In most individuals blood concentrations of the tetracyclines ranging from 1.0 to 3.0 μg. may be anticipated following doses of 0.25 gm. every 6 hours, while 2.0 to 4.0 μg. are usually observed following administration of 0.5 gm. every 6 hours. Blood concentrations of chloramphenicol following similar doses are higher, ranging from 2.0 to 4.0 μg. with the smaller dose and from 4.0 to 6.0 μg. with the larger dose (Figures IV and V.)

Although the broad spectrum drugs have a low sensitizing potential they do produce side reactions of varying degrees. The tetracyclines as a group may cause nausea, vomiting, and diarrhea and in some patients this can result in prolonged incapacitation. There is evidence also that oxytetracycline and chlortetracycline may provoke the emergence of resistant staphylococci in the intestines leading occasionally to a fatal septicemia. Because of the greater antimicrobial activity of chlortetracycline for the staphylococci, which is discussed later, this should be less likely to occur with it than with oxytetracycline.

An incidence of nausea, vomiting, and diarrhea varying from 3 to 30 per cent following broad spectrum therapy has been reported in the literature. These data did not include the newest of the broad spectrum drugs, tetracycline, which so far has shown considerably fewer side reac-

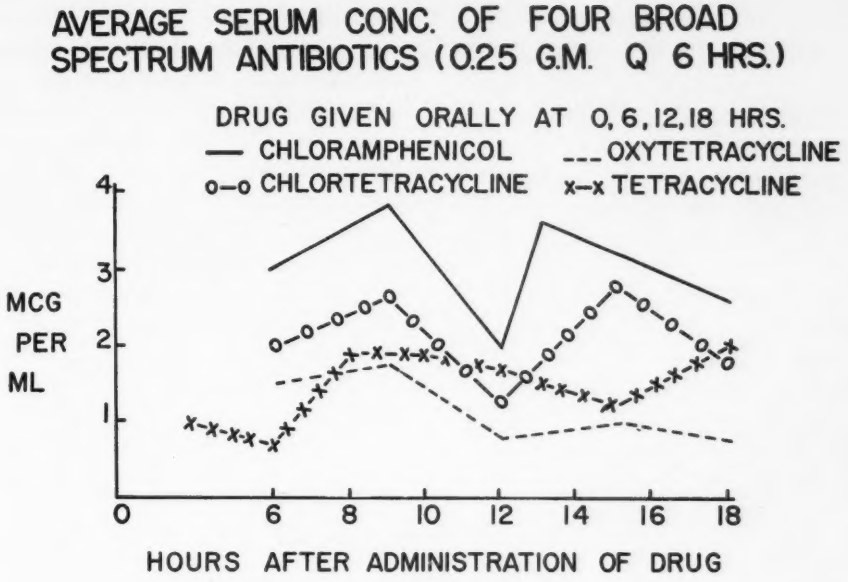

AVERAGE SERUM CONC. OF FOUR BROAD SPECTRUM ANTIBIOTICS (0.25 G.M. Q 6 HRS.)
DRUG GIVEN ORALLY AT 0, 6, 12, 18 HRS.
— CHLORAMPHENICOL ---OXYTETRACYCLINE
o–o CHLORTETRACYCLINE x–x TETRACYCLINE
MCG PER ML
4
3
2
1
0
6
8
10
12
14
16
18
HOURS AFTER ADMINISTRATION OF DRUG

FIG. IV

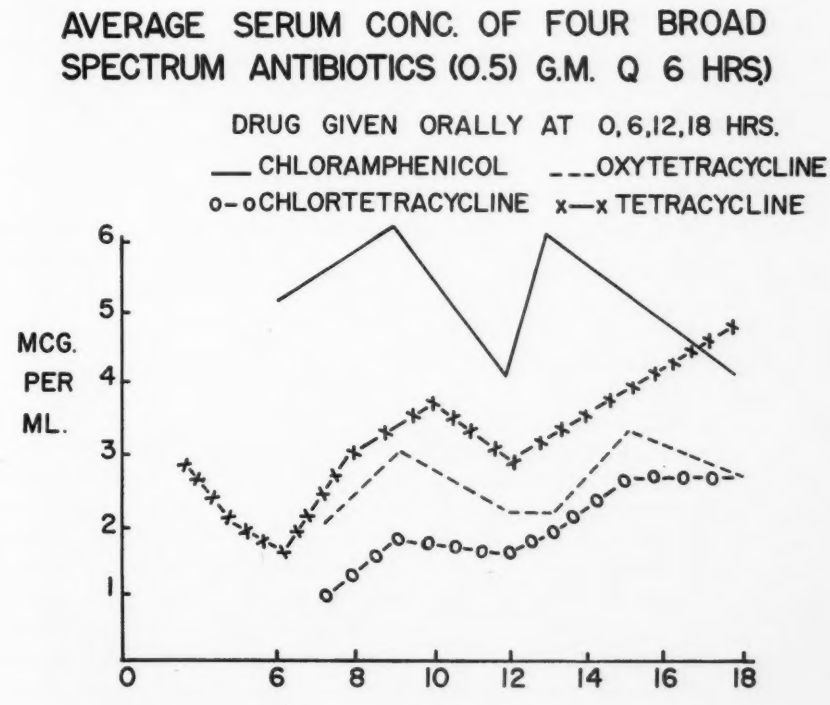

AVERAGE SERUM CONC. OF FOUR BROAD SPECTRUM ANTIBIOTICS (0.5) G.M. Q 6 HRS.)
DRUG GIVEN ORALLY AT 0, 6, 12, 18 HRS.
— CHLORAMPHENICOL ---OXYTETRACYCLINE
o–o CHLORTETRACYCLINE x—x TETRACYCLINE
MCG. PER ML.
6
5
4
3
2
1
0
6
8
10
12
14
16
18

FIG. V

	Tetracycline	Chlortetracycline	Oxytetracycline
Nausea	0	3	14
Nausea, Vomiting	4	16	10
Nausea, Vomiting, and Diarrhea	1	11	16
Diarrhea without vomiting	5	16	28
No side reactions	400	230	165
Total Patients	410	276	233
% Patients with Diarrhea	2%	10%	19%

FIG. VI. Untoward Reactions from the Tetracyclines

μg/ml.	Chlortetracycline	Tetracycline	Oxytetracycline
0.05	11	0	0
0.10	4	0	0
0.20	32	5	0
0.39	98	70	1
0.78	42 (187)†	121 (196)†	11 (12)†
1.56	28	27	105
3.12	13	5	62
6.25	3	0	38
12.50	5	0	7
25.0	7	1	0
50.0	7	4	0
100.0	19	36	45

* All coagulase positive.
† Total strains sensitive to 0.78 μg/ml. or less.

FIG. VII. Sensitivity of 269 Strains of *Staphylococcus aureus** to the Tetracyclines.

tions. From our own experience and that of others tetracycline is apparently the least apt to cause nausea, vomiting, and diarrhea, while oxytetracycline produces these reactions most frequently. Chlortetracycline has been reported recently to cause about one half as many of these reactions as oxytetracycline (Figure VI).

Since the recent preparation of tetracycline by catalytic hydrogenation of chlortetracycline and its production from a *Streptomyces* species by fermentation, large quantities have been made available for clinical use. The lower incidence of side reactions thus far reported with tetracycline has resulted in the suggestion in some quarters that it be substituted for the other two tetracycline drugs. However, in addition to the fact that many physicians have used tons of chlortetracycline and oxytetracycline with no difficulty and excellent therapeutic response, there are other factors to consider. It is true that preliminary studies have shown that an organism made resistant to one of the tetracyclines is similarly resistant to the others. Nevertheless, we have encountered organisms sensitive to one of these drugs and resistant to the others. This occurs with different species as well as with different strains of the same species. Several fold differences in the sensitivity of certain strains of *Staphylococci*, *Streptococci*, *Clostridia*, *Escherichia*, *Proteus*, *Brucella* and *Shigella* have been reported. In a study of 269 strains of coagulase positive staphylococci marked differences in sensitivity to the tetracycline drugs were found (Figure VII).

Of the 269 strains, 187 were sensitive to 0.78 μg/ml. or less of chlortetracycline, similarly 196 strains had the same sensitivity to tetracycline, but only 12 strains were sensitive to 0.78 μg/ml. or less of oxytetracycline. More strains of staphylococci were sensitive to low concentrations of chlortetracycline than to the other two drugs. Furthermore, while 19 strains were found resistant to 100 μg/ml. of chlortetracycline, 36 and 45 strains, respectively, were resistant to tetracycline and oxytetracycline.

If this relationship persists with other species of microorganisms—and some preliminary data indicate it will, it is highly questionable whether substitution of one for the other will accomplish the desired therapeutic effect. These data further emphasize the importance of in vitro sensitivity determinations.

From the time chloramphenicol was first discovered it was considered a drug which caused few side reactions. In comparison with oxytetracycline and chlortetracycline, chloramphenicol was by far the least likely drug to produce nausea, vomiting, or diarrhea. However, within about two years of its introduction clinically there appeared a few published reports concerning its role as an etiologic agent in the development of blood dyscrasias. As time went on, it

soon became evident that this drug in certain susceptible subjects caused serious blood dyscrasias.

The nitro-benzene radical of the chloramphenicol molecule has been suggested by some as the cause of its toxicity but the extremely low incidence argues against this possibility. One would expect large numbers of blood dyscrasias from this drug were it inherently toxic. Furthermore, development of a blood dyscrasia would be related to the dose administered. This has not been the case, since development of a dyscrasia following therapy with chloramphenicol has not been always related to the size of the dose. The fact that a large number of the dyscrasias observed followed administration of two or more courses of the drug makes it seem likely that it is related to a subtle and obscure sensitization phenomenon.

The reports of blood dyscrasias following use of chloramphenicol prompted a nationwide survey by the U. S. Food and Drug Administration in July and August of 1952. The survey covered mainly, although not entirely, cities of 100,000 population or more in 37 states. The data collected included all cases of aplastic anemia, granulocytopenia, and other blood dyscrasias that could be found since 1949; the name and quantity of each drug or chemical associated with the development of the disorder; the primary disease for which the drug was prescribed; the patient's history, blood studies, and other pertinent data.

A total of 539 case records were reviewed. These were classified into three groups: A. Chloramphenicol only known drug administered; B. Chloramphenicol and other drugs administered; C. Chloramphenicol not involved in the dyscrasia.

Of the 539 case records from 37 states, 55 had been administered chloramphenicol as the only known therapeutic agent during the preceding six months. Forty-four of these were diagnosed as aplastic anemia. Of 143 individuals treated with chloramphenicol and other drugs, including other broad spectrum antibiotics, anticonvulsants, antipyretics, or antihistaminics, 95 had a diagnosis of aplastic anemia.

		Aplastic Anemia
A. Chloramphenicol only known drug administered	55	44
B. Chloramphenicol and other drugs administered	143	95
C. Chloramphenicol not involved	341	157
Total cases reviewed	539	296

FIG. VIII. Chloramphenicol: 1952 Survey of Blood Dyscrasias.

There were 341 blood dyscrasias in which chloramphenicol was not involved and 157 of these were diagnosed as aplastic anemia. These data are tabulated in Figure VIII.

There was no conclusive evidence from this survey that the incidence of blood dyscrasias had increased since chloramphenicol became available. The dyscrasias were widely distributed throughout the United States and all age groups from infancy to the ninth decade of life were represented. Distribution by sex showed females predominating over males by about three to one.

Following this study and on a recommendation of the National Research Council, a warning concerning possible development of blood dyscrasias was required on the labeling of each bottle of chloramphenicol intended for systemic use. The adverse publicity given the latent toxicity of the drug in scientific journals, magazines, newspapers, television, and radio caused a precipitous drop in its use.

In the summer and fall of 1953 a second survey was made to determine the blood dyscrasias associated not only with chloramphenicol but with other drugs as well. This survey was more extensive and more emphasis was placed on drugs other than chloramphenicol which appeared to be related to blood dyscrasias. Furthermore, because of its very poor prognosis, greatest attention in follow-up was given to aplastic anemia.

A total of 1,448 case records were reviewed in the second survey. Each of the states except five contributed one or more cases and, as was to be

		Aplastic Anemia
A. Chloramphenicol only known drug administered	29	26
B. Chloramphenicol and other drugs administered	88	54
C. Chloramphenicol not involved	1050	137
Discarded	281*	
Total cases reviewed	1448	217

* 281 cases discarded because of lack of information or no evidence of actual blood dyscrasia.

FIG. IX. Chloramphenicol: 1953 Survey of Blood Dyscrasias.

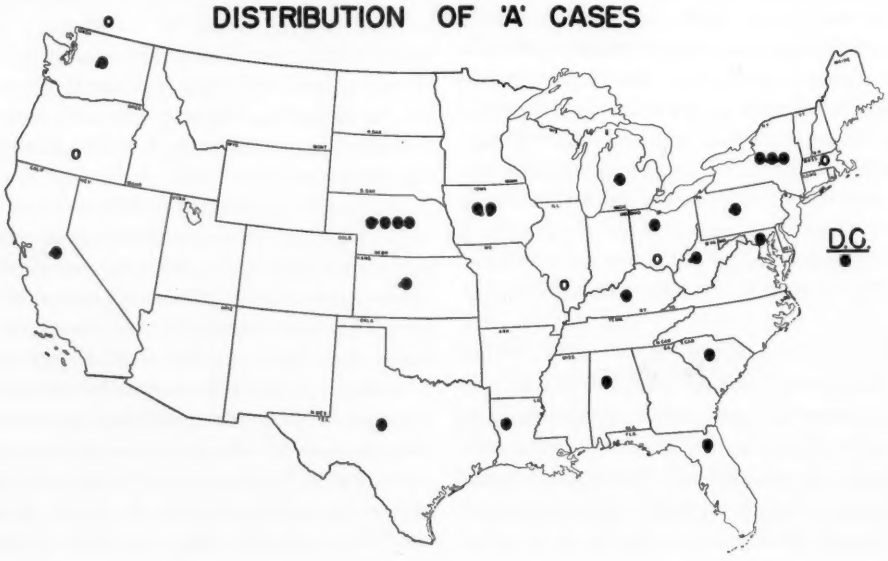
expected, most cases occurred in areas of greatest population. These data are shown in Figure IX and the distribution of cases throughout the country in the following three maps.

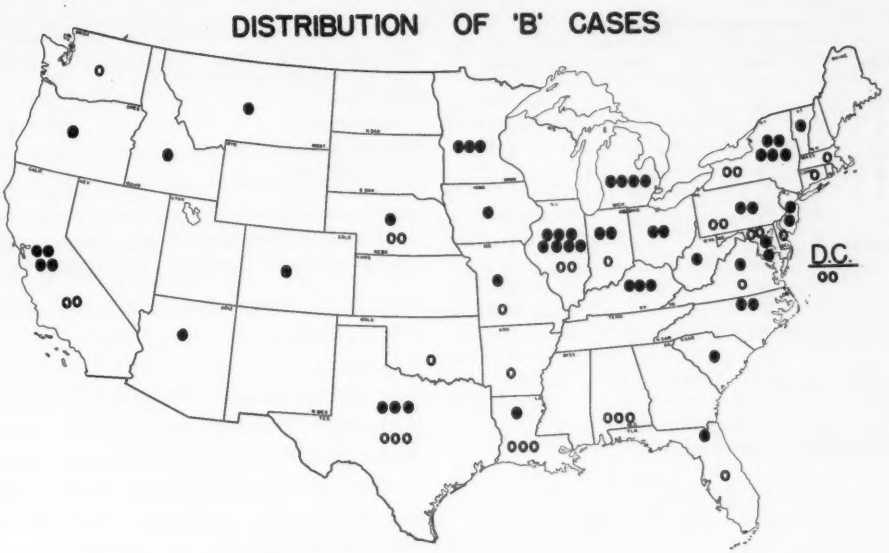
There were 29 blood dyscrasias classified in Group A (chloramphenicol only drug administered) and of these 26 were diagnosed as aplastic anemia. In Group B (chloramphenicol and other drugs administered) there were 88 cases and 54 of these were diagnosed as aplastic anemia. In Group C, in which chloramphenicol was not involved, there were 1,050 cases with 137 diagnosed as aplastic anemia. A total of 281 cases were discarded for lack of evidence of a blood dyscrasia or because sufficient data could not be obtained for classification.

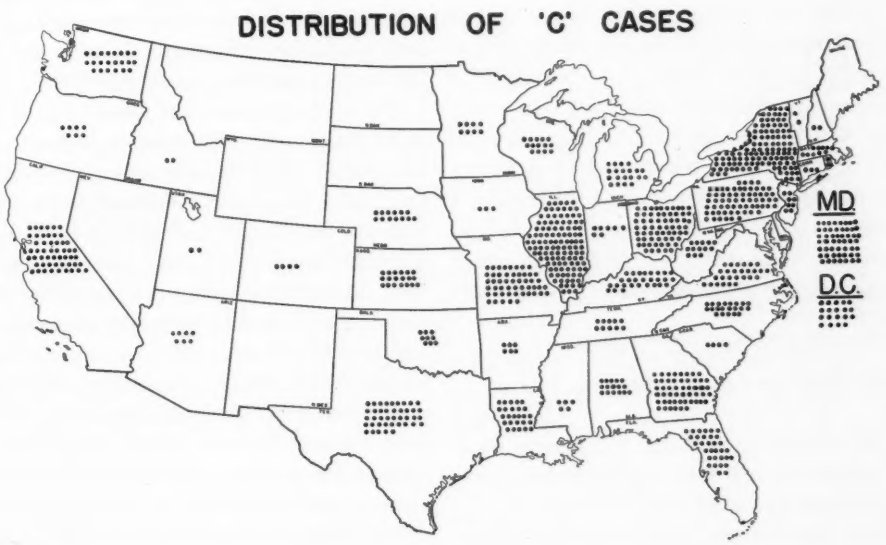
A preponderance of cases occurred within three months of the last exposure to the drug. Twenty-two of the total of 29 blood dyscrasias in the A group developed within this time interval. Females were more prone to develop blood dyscrasias than males. Of the 29 blood dyscrasias in Group A, 20 occurred in females, a ratio of about 2:1 as contrasted to a ratio of about 3:1 females over males in the 1952 survey. At the completion of the 1953 survey 21 of the 29 classified in Group A were dead. These data are shown in Figure X.

In Group A cases of 26 patients whose exact age was known, 17 were under 10 years of age when their blood dyscrasias were diagnosed. Five other blood dyscrasias occurred in patients 50 to 70 years of age. The incidence of blood dyscrasias at various ages for the "A" group of cases is shown in Figure XI.

It was important to determine whether chloramphenicol had been administered to the Group A and B cases prior to or after the warnings and wide publicity received by this drug. This analy-







sis showed that of the 29 Group A cases, 22 had received all of their drug (one or more courses) prior to the wide publicity given it and also prior to the required label warning. Of the remaining 7 cases there were 6 to whom chloramphenicol was administered both before and after that time, while only one patient received all of the drug afterwards. This case was a dentist who, on his own initiative, took several short courses of the drug for the treatment of "colds." He subsequently died of aplastic anemia. Thus, the second survey uncovered in the A group only one blood dyscrasia where all the chloramphenicol had been taken after the warning of its possible danger,

Group "A" Cases

Months	Total	Male	Female
<1	8	1	7
1–2	8	1	7
2–3	6	2	4
3–4	1	1	0
4–5	2	1	1
5–6	1	1	0
Unknown	3	2	1
	29†	9	20*

* Previous survey 55 "A" cases, 41 females, 14 males (3:1).

† 21 dead at completion of survey.

FIG. X. Onset of Dyscrasia after last Exposure to Chloramphenicol and Sex Distribution

Group "A" Cases

Years	Cases
0–4	10*
5–9	7
10–14	1
15–19	1
20–29	0
30–39	2
40–49	2
50–59	3
60–69	1
70–79	1†
	28‡

* 8 aplastic anemia, 2 thrombocytopenic purpura.

† 1 anemia (severe).

‡ 1 adult, exact age unknown, not included.

FIG. XI. Blood Dyscrasias in Different Age Groups.

and in this instance without the benefit of a physician's advice and for a condition for which the drug should probably never be used.

Similarly, most of the cases in the B group received their drug either prior to the warning or prior to and after it. Sixty-one cases were administered chloramphenicol prior to the warning and 11 more got the drug both before and after, while only 16 received all of their drug subsequent to the warning and wide publicity concerning its ability to cause blood dyscrasias.

	Patients	Alone*
Coal Tar Analgesics; Salicylates	14	4
Sulfonamides	14	4
Antihistamines	15	0
Streptomycin; D H S M	5	3
Chlortetracycline	11	2
Oxytetracycline	12	4

* Number of cases in which these were the only drug or drugs administered along with chloramphenicol.

FIG. XII. Aplastic Anemia: Collateral Drug Association of 54 "B" Cases.

In Group B other drugs were administered along with chloramphenicol. There is no way of determining whether these collateral drugs were involved in the development of the blood dyscrasias, and only by inference can we say that chloramphenicol alone is responsible.

Because of the poor prognosis of aplastic anemia, the 54 cases in Group B have been classified according to collateral drug association. These data are shown in Figure XII.

Coal tar analgesics and salicylates were used in 14 cases along with chloramphenicol and in 4 of these no other drugs were used. Similarly, sulfonamides were used collaterally with chloramphenicol in 14 cases and in 4 of these no other drug was used. In 15 cases antihistamines were used along with chloramphenicol. In 5 cases streptomycin or dihydrostreptomycin were used collaterally and in 3 of these no other drug was involved; in 11 cases chlortetracycline was used and in 2 of these it was the only drug used other than chloramphenicol; while in 12 cases oxytetracycline was used collaterally with chloramphenicol and in 4 of these no other drug was used.

The aplastic anemia cases in Group C have been classified as to their drug association (Figure XIII). These cases do not involve chloramphenicol.

A total of 20 cases were administered antibiotics other than chloramphenicol either alone or with other drugs. Nine received oxytetracycline and in 2 cases it was the only drug ad-

ministered; 6 received chlortetracycline and in 1 it was the only drug given; and 5 were administered streptomycin but in no case was it the only drug used.

Twenty cases were given coal tar analgesics or salicylates and 5 received these drugs only; 8 were given anticonvulsants and in 5 these drugs only; 4 received antihistaminics, in 1 these drugs only; 15 received barbiturates, in 2 these drugs only; 4 received heavy metals, in 2 these drugs only; 9 were exposed to weed killers or insecticides and in 6 this was the only exposure to drugs or chemicals; organic solvents were involved in 14 cases and 10 of these were apparently due to benzene; 22 cases involved the sulfonamides and in 11 these were the only drugs used.

There were some miscellaneous associations in the Group C aplastic anemia cases. Nitroglycerine, antimalarials, furniture wax and polish, desoxyephedrine derivatives, chemicals, dormison, hair rinse and hair dyes, demerol, and x-ray and radium were all associated frequently with other drugs. However, in 11 cases these preparations were not associated with the use of other drugs nor with exposure to chemicals. These data are shown in Figure XIV.

The variety of drugs associated with aplastic anemia in Group C which excludes chloramphenicol from consideration emphasizes the problems inherent in chemotherapy. If we use the same criteria with these drugs as we did with chloramphenicol then they would be placed in the class of hemopoietic poisons. Although some of these drugs have been involved in blood dyscrasias previously the majority have not, and we therefore are forced to label the dyscrasias as "probably idiopathic," a questionable procedure. On the same basis, however, there are undoubtedly cases in Group A where chloramphenicol alone was administered that were also "probably idiopathic" and would have occurred whether the drug had been administered or not.

The low incidence of blood dyscrasias generally raises the question as to whether many are not associated with a subtle and obscure sensitization phenomenon in some individuals which is "triggered" by certain classes of drugs. Some drugs have a greater sensitizing potential than others. In addition, the individuals involved would perhaps be those most prone to develop a sensitivity; the asthmatics and others already sensitive to drugs, foods, bacteria, or pollens. It is also of interest in the case of chloramphenicol that children are most frequently involved and

Chloramphenicol Not Involved

	Patients	Alone*
Oxytetracycline	9	2
Chlortetracycline	6	1
Streptomycin	5	0
Coal Tar Analgesics; Salicylates	20	5
Anticonvulsants	8	5
Antihistamines	4	1
Barbiturates	15	2
Heavy Metals	4	2
Insecticides and Weed Killers	9	6
Organic Solvents (Benzene 10)	14	
Sulfonamides	22	11

* Number of cases in which these were the only drug or chemical exposures.

FIG. XIII. Aplastic Anemia: Drugs Associated in "C" Cases.

Chloramphenicol Not Involved

	Patients	Alone*
Nitroglycerin	4	3
Antimalarials	3	0
Furniture wax, polish	3	1
Desoxyephedrine derivatives	7	1
Chemicals	3	3
Dormison	4	1
Hair Dye, Rinse	2	1
Demerol	3	0
X-ray and Radium	3	1

* Number of cases in which these were the only drug or chemical exposures.

FIG. XIV. Aplastic Anemia: Miscellaneous Drugs Associated in "C" Cases.

Chloramphenicol Not Involved

	Cases	Number Idiopathic
Hypoplastic Anemia (Pancytopenia)	126	64
Anemia (Refractory or Hemolytic)	37	11
Thrombocytopenic purpura	499	266
Non-thrombocytopenic purpura	8	1
Granulocytopenia or agranulocytosis	79	7
Leucopenia	32	3
Total cases	781	352

FIG. XV. Blood Dyscrasias Other Than Aplastic Anemia in the "C" Group.

females are affected two to three times more frequently than males.

There were 781 blood dyscrasias in addition to the aplastic anemia cases where drugs other than chloramphenicol were used. These included 126 cases of hypoplastic anemia, 37 cases of refractory or hemolytic anemia, 499 cases of thrombocytopenic purpura, 8 cases of non-thrombocytopenic purpura, 79 cases of granulocytopenia or agranulocytosis, and 32 cases of leucopenia. Of these, a total of 352 cases were classified as idiopathic (Figure XV).

When chloramphenicol was first studied, and for a long time thereafter, it was considered to be the least toxic of the broad spectrum drugs, at least from the standpoint of gastro-intestinal disturbances. It was this low incidence of side reactions that may have provoked its wide and unfortunately unwise use in many instances. However, it should have been recognized that as a drug of considerable potency and potential for good, it, of necessity, could be harmful under appropriate conditions in certain individuals. There seems to be no question now that on rare occasions in susceptible individuals under certain conditions chloramphenicol causes serious blood dyscrasias. It is to be regretted that we cannot define these "conditions," but repeated exposure does appear to carry an increased hazard. There is general agreement that penicillin is probably the least toxic of the potent chemotherapeutic agents now in use, yet we have reason to believe that it is responsible for from 100 to 200 acute anaphylactic-like reactions in a single year and the number appears to be increasing. While it is true that in this anaphylactoid type of reaction an adequate history and sensitivity tests may afford a means of prevention, these are not infallible. It must be concluded that the decision to use chloramphenicol or penicillin, or for that matter any potent drug, must rest with the physician who through clinical judgment balances the drug's potential to do harm against the seriousness of the condition under treatment.

If the total cases of blood dyscrasias in the A groups from both surveys are combined, we find that chloramphenicol was the only drug used in 84 of the 1,706 reviewed (4.9 per cent). In addition, in the second survey over 60 per cent of these dyscrasias occurred in children under 10 years of age.

Of special interest are the cases in category C. These patients had never taken chloramphenicol, or it was administered only after the blood dyscrasia was already well established. Of this entire group we can say with reasonable certainty that chloramphenicol was in no way involved in the development of the blood dyscrasia. There were 269 cases of aplastic anemia in this group and of these 137 were classified as idiopathic.

In the final analysis it seems likely that some of the cases of aplastic anemia which have been attributed to chloramphenicol, or other drugs for that matter, actually represent idiopathic cases and that the association with any drug is mere coincidence. It is noteworthy that very few of the cases of aplastic anemia encountered in either of our surveys actually had a complete blood count just prior to the time the suspect drug was started. It should be emphasized that it cannot be stated with finality that chloramphenicol, or any of the other drugs discussed in this report, actually caused the blood dyscrasia which developed following their use.

To summarize the second survey, its primary purpose was to determine whether or not the warning now required in the labeling of chloramphenicol is adequate for the safe and effective

use of this drug. The National Research Council in 1952 felt that it should be, and this survey, in our opinion, further supports their judgment. From the information we have gathered there is every reason to believe that the medical profession has been alerted to the possible hazards involved when this drug is employed so that the decision to use it rests with the physician where it properly belongs.

Division of Antibiotics,
Food and Drug Administration
Dept. of Health, Education and Welfare
Washington, D. C.

Psychiatric Panel

BRIEF MEDICAL PSYCHOTHERAPY AND THE QUESTION OF THE PSYCHIATRIC REFERRAL[1]

KLAUS W. BERBLINGER, M.D.[2]

During the last fifteen years, psychiatrists have made a concerted effort to make their concepts and methods of treatment applicable to various medical specialties. By comparison with a number of other fields of medical endeavour, the general practitioner has the distinct advantage of more intimate contact with his patient's cultural, social and economic surroundings. He is, therefore, capable of better assessment of a connection between illness and problematic, emotional constellations, and has the unique opportunity to serve his patient not only during the "temporary decompensation" of a prevailing illness but can act as a continuum of therapeutic and prophylactic care. Thus, the general practitioner can be the exponent of a modern concept in medicine which considers the family group as a unit in sickness and health. This concept is often referred to as "comprehensive medicine." Application of this concept means to concern oneself with multiple aspects and factors influencing an individual's illness.

This discussion is concerned with the psychologic or emotional variables as they contribute to illness. Their importance and frequency no longer needs particular emphasis. However, while the scope is known, the practical management of just these factors is more often than not left to talent, intuition and improvisation, and the inclusion of psychotherapy appears to many physicians merely on the periphery of teachable, scientific medicine.

Only during the last decade, a term like "medical psychotherapy" has been devised and subjected to the scrutiny which any method of treatment deserves. In slight modification of an earlier definition (Greenhill) one may say that "medical psychotherapy denotes that aspect of medical treatment in which personal interaction between doctor and patient constitute an intended and principal therapeutic agent." This characterizes the agent as a field of operations between patient and physician in which mutual reactions and counterreactions result in a relationship of therapeutic significance. Admittedly, no relationship can be established without some form of communication between the persons involved. Communication may be confined to verbal exchange or may include all levels of a person's physical expressions which convey information about his presence. At any event, it

[1] Presented at the One Hundred and Fifty-sixth Annual Meeting of the Medical and Chirurgical Faculty of the State of Maryland, on Tuesday morning, April 27, 1954, in Osler Hall, 1211 Cathedral Street, Baltimore 1, Maryland.

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can be utilized as a measuring device to describe what happens between physician and patient. Consequently, one can define the process of psychotherapy by observation of communicative devices and thus clarify the roles which the participants assume. Such clarification seems indispensable for evolving a teachable method.

Manipulative vs. Insight Therapy

Traditionally one distinguishes in psychotherapy between methods of manipulation and those of insight treatment, and one delegates the more manipulative processes to the non-psychiatric specialist, while insight therapy is considered the prerogative of the psychiatrist. The preceding emphasis on the process of interaction may serve to draw such rigid borderlines into question. Manipulation implies the time honored custom of taking active influence on external stresses, for instance by an advice to change climate, occupation or social ties. On the other hand, insight should denote a development during which a patient becomes aware of his underlying motives and learns to relate these motives with his actions. Such insight, if achieved under psychotherapeutic guidance is certainly not entirely independent from the guiding spirit, and, by the same token, results of seemingly manipulative measures are equally influenced by a relationship which exists between the counselled and the counsellor. With this in mind, it may be permissible to forego description of various, individual techniques and to dwell upon a number of occurrences universal to all psychotherapeutic activity:

Establishment of a Relationship

Our first problem is the establishment of a relationship in which measures and solutions become acceptable and of value to the patient. It is here where method begins to differ from intuition. The latter often consists of asking oneself "how would *I* feel in this patient's shoes?" and then to arrive at a decision which would implicate the doctor in a range of situations and emotions, probably beyond anybody's capacity. And even if the physician were able to live through such a range of feeling for his patient's sake, the therapeutic experience would be not the patient's but his physician's. It so becomes obvious that also in psychotherapeutic medicine the goal should be the patient, never the doctor. Technically, this is accomplished by focusing attention and discussion on symptoms, topics and material which the patient indicates (Finesinger). A sound or a facial expression of pain takes precedence over the physician's difficulty in finding the spinal canal, a casual remark as to the circumstances surrounding the onset of a symptom, rates immediate priority over the diagnostic significance of the location of any specific discomfort. Therefore, in order to establish and to maintain a meaningful or positive relationship the doctor has to acquaint himself with observation and evaluation of a patient's communicative means, be they physically noticeable or verbally implied.

Maintenance of a Relationship

The maintenance of such relationship is assured when the physician proves himself adept in dealing with the patient's problem in terms of the meaning it has to the patient. If a mail carrier loses a foot by amputation, he will attribute to the loss a different significance than a bank clerk; a father of eight children will view difficulties with his boss in a more consequential light than a bachelor without encumbrances. It follows logically that the physician finds himself no longer in a role of judge or medical plenipotentiary, but has become a participant observer who has to be continuously mindful of his own feelings toward the patient and his affliction and of the impact which his presence, conduct and counsel will make. Such introspection may include even the reasons for which we became physicians and considerations of the particular field of application in which we ultimately find ourselves.

Advantages, Limitations and Pitfalls of Relationship

If we now consider the established relationship as the rails on which our treatment effort moves, we have to survey its advantages, limitations and pitfalls. On the positive side, it is apparent that clarification of communication, in other words mutual understanding between doctor and patient, will help diagnosis, management and acceptance of any medical situation. To feel understood results in greater freedom to reveal, willingness to follow necessary measures and may promote recovery. Such a positive, almost ideal interaction is, however, not immune to difficulties inherent in traits the patient—and sometimes also his physician—have brought into the relationship. "Trait" denotes these factors as something which has been previously acquired. Their recognition requires not only familiarity with general psychopathology but the ability to correlate the results of our immediate observation with habits, attitudes and behavior characteristics which the individual may have had prior to his illness. The most frequently encountered stumbling blocks in a process of good relationship concern problems of dependency which the patient may either reject or may be all too willing to accept. The physician—for reasons of his own—can unwittingly foster or deny such tendencies. He may become a dependency symbol or substitute. The degree to which he allows himself to enter such a role, is often determined by the severity of an illness, but may also be inherent in his own personality. The resolution of dependency conflicts is notoriously difficult and remarks about the psychiatric referral might find here their place!

Psychiatric Referral

At last year's meeting of the American College of Physicians, Dr. Brosin intimated to his colleagues that during certain crises in medical management, a patient might profit not so much by referral to a psychiatrist but by a conference between his physician and a psychiatrist. Dr. Brosin obviously alluded to a relationship crisis, and since a great number of referrals originate in just this area, observations of reasons for psychiatric referral may be in order.

In referrals for predominantly physical manifestations of an illness, feeling can be controlled by attention to some concrete detail of medical technique, anatomical or physiological outline. Such a barrier to one's feelings is more difficult to maintain when it concerns the intangible, abstract reverberations of mutual emotions. Therefore, it may be of some help to group the occurrences during psychiatric referral under three headings: motivations, attitudes and expectations. All of these include the physician. Just with as much justification as we expect in the case of a surgical referral, must we ask ourselves "Why" the physician asks for a psychiatric consultation at any given time. (I am here purposely avoiding the situation of psychotic patients who are obviously out of contact with sound reality. In such cases usually no great problem is encountered.) Our second question considers the physician's attitudes at the time of such a referral, and finally, again just as in any other referral we may inquire about the expectations. During a recent study, extending over a period of four years, an opportunity existed to assess some of these factors. The study was conducted first within the confines of a teaching hospital (Greenhill-Kilgore), later on, extended into a situation of private practice and contact with a defined group of practitioners. It became apparent that a number of motivations, attitudes and expectations not only governed the act of referral, but significantly influenced the resultant relationship with the psychiatrist. In analysing what seem rather pertinent data, in order of their frequency, the following motivations were found: Rejection, identification and the attempt to bring the patient into a treatment best suited to his needs. Clearly, only this last motive could be considered free from unnecessary obstacles.


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[1]January, H. L. et al: Clinical experience with tetracycline. *Antibiotics Annual* 1954-55, p. 625.

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Motivations

It was observed that physicians seemed inclined to favor detaching their patients at the time of referral. It is almost unnecessary to state that such feeling and intention cannot escape detection by the patient who then suffers the pain of what we prefer to call, passive rejection. This tendency to steer the patient away was noticeable in statements made at the time of referral, unwillingness to re-enter the treatment process, failure to inquire into progress or refusal to participate in aftercare.

Another, equally dubious motive for referral constituted persistent identification between physician and patient. Actual or imagined similarity between problems encountered motivated psychiatric consultation and had presented a stumbling block for a detached professional relationship. Once this was recognized, treatment with the previous therapist often became feasible again and made the referral unnecessary.

Attitudes

Attitudes observed even more openly indicated the doctor's role and the degree of his own anxiety in deciding on referral. Whenever a physician seemed to be free from undue anxiety about nature and purpose of psychiatric care, he seemed able to be rather direct about his intentions and then little opposition was encountered. However, with unfortunate frequency the referring attitude could be classified as "disdainful, apologetic, interfering, discouraging, reluctant or circuitous." The last is illustrated by the case of a patient who is led to expect consultation with a neurologist, but in our age of mass information media, sooner or later discovers that he is seen by a psychiatrist. Usually the patient reacts with further loss to his self esteem, for he rightfully considers his balance of mind precarious if his physician does not trust him with being able to "take it." The ensuing resentment is usually directed against referring physician and psychiatrist alike and chances for successful psychotherapeutic cooperation become anything but hopeful. Such attitudes may reflect previous experience a physician had with similar referrals, but it is also suggested that they infer deeper problems of his own.

Expectations

Expectations from psychiatric treatment run the gamut from overpessimism to an overoptimistic appraisal of psychotherapeutic prospects. Statements like "go to Doctor Soandso and get yourself analyzed," may sound like lack of information, they may reflect popularized and oversimplified concepts. But perhaps they may also be overcompensations of a doubtful mind and are thus akin to overpessimism. The realistic view that such treatment is necessary and probably will improve matters to the extent of making the unbearable more tolerable, is not always the prevailing one.

Summary

Medical psychotherapy is treatment through personal interaction or relationship. It is a natural field for the general practitioner who is closer than any other specialist to his patient's needs and who alone, can provide the continuity of therapeutic and preventive medical care. To perform this task with scientific accuracy, the concept of process in human interaction is stressed and some of its multilateral factors, like self awareness, familiarity with communication techniques and psychological response pattern are enumerated. In discussing the psychiatric referral, problem areas of the physician under the headings of motivation, attitude and expectation are described.

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References

Berblinger, K. W., Medical Psychotherapy, Virginia Med. Monthly, **78**, 259, 1951.

Berblinger, K. W. and Greenhill, M. H., Levels of communication in ulcerative colitis, Psychosomatic Medicine XVI, **2**, 156, 1954.

FINESINGER, J. E., Psychiatric Interviewing: Some principles and procedures in insight therapy, Am. J. Psychology, **105,** 187, 1949.

GREENHILL, M. H., Application of psychosomatic techniques to the general practice of medicine, North Carolina M. J., **10,** 535, 1949.

GREENHILL, M. H., FITZPATRICK, N. W. AND BERBLINGER, K. W., Recent developments in the teaching of comprehensive medicine, North Carolina M. J., **11,** 615, 1950.

GREENHILL, M. H. AND KILGORE, S. R., Principles of methodology in teaching the psychiatric approach to medical house officers, Psychosomatic Medicine, **12,** 1, 1950.

WHAT MIGHT THE PRIVATE PRACTITIONER EXPECT OF THE PUBLIC PSYCHIATRIC HOSPITAL?[1]

CLIFTON T. PERKINS, M.D.[2]

In speaking on the assigned topic I have rather clearly in mind some of the great responsibilities which fall upon the broad shoulders of the private practitioner—particularly the family doctor. Of course, he is supposed to know about all there is to know about the family and the sick individual. He is supposed to be skilled in the scientific diagnostic and treatment methods of today. And, of course, he is supposed to know the habits of the patient, his personality, his relationships with members of the family and the community, and to know all of the community resources available which will help him in maintaining or restoring the health of his patient. That is a tremendous responsibility. In order to fulfill it adequately, he cannot be expected to rely upon cold formulae. Rather, he must depend upon his individual judgment and his knowledge of the various resources available to him and how to use them. And in respect to the latter, in particular, he must have confidence in the resources of help to his patients.

Those are a few of the major challenges, as I see them, which are posed for the family physician to meet. And they pose similarly great challenges, in the field of the mentally ill, for the state and the administrator of public psychiatric services to meet.

At this point I pause to remind myself of the state responsibility in regard to the care of those mentally ill who require hospitalization. True, for 97% (or more) this becomes a state responsibility. It is largely a state monopoly. And it is state medicine—using that term in its generic sense. It has been this for one hundred years or more, and in the light of our present knowledge it is likely to be a major state responsibility for an indefinite number of years to come. This seems a probability if for no other reason than the very simple fact that most mentally sick people just cannot afford private care. Thus, in the statutes accepting this great responsibility, the state has posed a major challenge for itself to meet.

Now, bearing in mind the responsibility of the family doctor to his patient and the family, and having clearly in mind the responsibility of the state to help as far as possible, let me take you on a quick kaleidoscopic view—somewhat step by step—of how I feel that the state is trying to meet a fair share of that responsibility at this time, and how I hope that our mutual efforts may be improved in the future.

1. *Admission.* First of all is the question of how to get a patient into a hospital. The family doctor has a right to expect that he may be able

[1] Presented at the One Hundred and Fifty-sixth Annual Meeting of the Medical and Chirurgical Faculty of the State of Maryland, on Tuesday morning, April 27, 1954, in Osler Hall, 1211 Cathedral Street, Baltimore 1, Maryland.

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to have a sick person admitted to a hospital with a minimum of red-tape. I think that is provided in Maryland. Of course there have to be certain safeguards in regard to the rights and protection of sick persons who are incapable of legally speaking for themselves. But by and large, the commitment laws of Maryland are very liberal in permitting medical judgment to be paramount. Our commitment laws may leave something to be desired, but for the medical profession they are far less burdensome than the restricting laws of most other states. And for the patient, our commitment laws eliminate many of the emotional hazards which accompany the process of commitment in many of our sister states. For the family doctor in particular, I am well aware that there still exists some confusion in regard to the procedural steps in connection with proper admission of a patient. After a long process of work, clearing of forms, checking proper legal implications, etc., we have recently completed a simplified MANUAL OF COMMITMENT which we will cause shortly to be placed in the hands of health officers and others ultimately concerned with admission procedures, and which we plan to make available for the general medical profession through appropriate channels including medical libraries and possibly through the medium of the Journal. In this manual, the legal requirements are cited, the form to comply with those requirements is reproduced, and accompanying these there is a brief narrative of simplified, common-sense material in an effort to be more helpful to the physician who has a patient requiring mental hospital care.

Also, in regard to admissions, all so-called "waiting-lists" have been abolished. I realize that this has raised some criticism when one remembers the increased overcrowding which this policy has thrust upon our public hospitals. But as a medical administrator, I cannot help but feel that it is more humane, more economical in the long run, and much more in accordance with good medical practice, to take care of the very sick mental patient in even an overcrowded and understaffed mental hospital than it is to try to care for him in an overcrowded, undermanned, and perhaps unsanitary home of low economic status. It was that basic thought, after some two years of special study, that caused us to eliminate all waiting lists.

Of course, ordinary admissions have certain procedures to follow, which we are not at liberty to circumvent. But emergency admissions are taken at any time—and the so-called "red-tape," or procedures of meeting the usual commitment requirements, straightened out as soon as possible after admission.

Thus, the first requirement of the family physician—for ready access to the hospital for a very sick person—has been met to a considerable degree by the public hospital.

Once the patient is in the public mental hospital, the question of what sort of services are to be provided for him is of considerable concern to the referring physician. It is these services and facilities which largely provide appropriate professional recognition for the hospital.

2. *Capital Improvements.* The family physician has a right to expect that his patient will receive certain physicial surroundings which will help his patient get well and to live within reasonable limits during the time that treatments are being undertaken. This calls for steps to overcome the problems posed by overcrowding and by the absolute necessity of separating sick people into general groups according to diagnostic and therapeutic requirements; and to improve food services and hazards of health and safety; and improve the general living conditions; and to provide facilities which help to minimize or entirely eliminate waiting lists where sometimes families have had to endure the heartbreaking tasks of trying to care for very sick loved ones at home. All of these factors are basic to any treatment program, and the family doctor has a right to find them in a public mental hospital as he would expect to find them in other hospitals. Not that buildings and improvements are, by themselves, the all-important thing, but they are

necessary as the foundation for good medical work. And sometimes the state is apt to forget, and the family doctor has to remind us, that, in the very nature of mental illnesses, the hospitals are also homes for the patients, too—not for a week or ten days, but for many months, and too often even for years. And the family doctor has a right to expect that his patients have a roof that doesn't leak over their heads; that they are in buildings suited to their needs—buildings which are sanitary, modern, and relatively free from the hazards of fire and health; and food service consistent with the special medical requirements of the patient and consistent with the general level of eating habits of the majority of Maryland citizens. All of these things, obviously, help to maintain the self-respect of the sick person and provide the treatment teams with the environmental factors so important to their work.

The progress of this part of the program in Maryland should be of some encouragement to the family doctor.

3. *Day-to-Day Care.* And the family doctor, in his role having special concern for the sick person in relationship to his family and the community, realizes that the public mental hospital may have to serve as the home for his patient for a long period of time. And so he would expect the hospital to be maintained in accordance with the standards of good care at home or in some other type of hospital. That is, he would expect the buildings to be kept in repair, and that heat and plumbing and other facilities for purposes of convenience and health and safety for daily living would be maintained properly. That requires much personnel and much money. And he would expect good day-to-day care by attendants who are so important for that loving care for the sick who are a long way from loved ones at home. He would expect good cooks to prepare good food, and have it well-served. And he would expect cleanliness of wards and linen. These things are so obvious that I almost apologize for even mentioning them. But they are very important. And they take much personnel at great cost. They are basic for the care of any sick person—at home, or in any type of hospital, especially so in a public mental hospital.

While we have tremendous personnel problems from time to time—almost incessantly—the state is trying hard to meet those simple and basic requirements which any family doctor has a right to expect for his patient.

4. *"Brain-Power."* Now, of course, all of these things are important to a public mental hospital as it tries to fulfill the expectations of the family doctor. Of course he wants his hospitalized patient to be in a safe place where the roof isn't going to leak; and he wants his patient to receive good and proper food; and to be kept warm and comfortable; and to reside in clean surroundings; and to have his daily personal needs met. But most of all he wants to be sure that his patient will receive excellent treatment, become well, and leave the hospital—as soon as possible. That means that when he turns his patient over to the public hospital he expects the patient to be in the hands of good doctors who are experts in their field—not novices, with all which that implies. And he has every reason to hope that, with reasonable diligence, the hospital doctors will determine the cause and nature of the illness, and will take such expert steps and time as necessary to cause a treatment program to be outlined and followed so as to restore the patient to health as soon as possible.

Of course, this requires that large bulk of professional people and subprofessional people who make up the treatment teams—physicians, dentists, graduate nurses, social workers, psychologists, rehabilitation experts, and technicians and consultants in many different categories.

That is where a tremendous amount of our money is going today. That is where we are putting our greatest emphasis. Oh, I do not mean to imply that our public hospitals have reached utopia—not by any means. But we have gone far, and each year more and more and

better and better professional people are being added to our staffs. That should be a source of some encouragement to the family doctor faced with the mental patient who requires hospital care.

Perhaps you have heard or seen something of so-called "back ward" patients. Perhaps some of your patients have been numbered among them. Well, they are the people who represent our medical failures. They form our human "salvage yards." Our failures in the Public Mental Hospital continue to live on and on, and reside on these less desirable wards, always under foot and a thorn in our side—always a reminder that we don't know as much as we should about their illnesses, and that we do not have the necessary treatment teams to utilize fully even that limited knowledge which we do possess. We cannot tackle the challenge of that group of the very sick without adequate treatment teams, coupled with research—of which I shall speak in a moment.

Of course, the problem posed in this "brain-power" question is the bottle-neck with which we are stuck. I'm sure it is familiar to all of you. That is, the shortage of trained people and the shortage of experienced people who can train the untrained. It is a problem with which your own Committee on Medical Care is wrestling earnestly to help find an answer, particularly in the nursing field. I will not burden you with figures, but will simply call to your attention that the overall national shortages for professional people in the field of the mentally ill, are tremendous. That means just two things—competition and training.

Competition in our field is very great. And the more we run up against it, the more we realize that sick people just aren't in a position to wait for the downswing of the economic pendulum and the upswing in the supply of trained people. An economic bull market for private work is always an economic bear market for the public mental hospitals—and especially in the professional and sub-professional fields. Of course that means competition, and we are consistently urging the state to meet that competition wherever it exists and at any reasonable level! Again, sick people can't postpone their illnesses to a "better day."

5. *Training and Research.* The training of people in the professional and ancillary fields is, obviously, a MUST. That training is going on at the present time in many different fields. Each year it is improving in quality, in scope, and in curriculum content, and is increasing quite noticeably in the numbers involved. It is a very encouraging sign. It offers a means of providing better care and service at the time. And it is a means of providing a reservoir from which to draw persons for expanded services and for future replacements. Naturally, an important by-product of training is the stimulation provided for the resident staff. Such a program is keyed to helping get more people well today, as well as to look forward to helping the sick many years from now. Our training programs already have extended to include affiliations in some fields with several hospitals and other agencies in some of our sister states in the south.

Of course, research is encouraged—research in the medical and ancillary disciplines in both basic and clinical matters. Such research forms an outlet for the brains available so that they might find interesting and useful channels for their abilities along lines which will ultimately provide high benefits for the sick today and for our statistical patients in the future.

One very definite place where the whole field of mental illness has lagged in research is among those who have mental illness coincident to advancing years. From a medical and humanitarian point of view, as well as from the question of economics, this group of elderly patients is very important. It is urgent that we know something more about them. You see, progress in many fields of medicine over the years has been building bodies that have outlived their minds—has been building chassis that outlive the igni-

tion. And we in the field of administering public mental health programs, depending on public support and understanding as our patrons for research, have not kept pace. It has not been easy to interest public support in this direction, although the ice has been broken a bit.

Private industry and private medical services have learned the benefits of research and training They spend millions of dollars annually in these fields. Why? Probably not alone because someone pulls the heartstrings about the needs of an unfortunate patient—rather, I suspect, more because it pays in the long-run, and because it is an accepted note of progress, and because competition demands it. In the care of the sick in a public mental hospital, should the state do less? We are trying to do more and more each year, and we are receiving increasing support from the coordinating agencies and key people in the executive and legislative branches of the state government.

There, in a rather quick look, are some of the major programs which the State is pushing forward for the care of the mentally ill who require hospitalization in the public mental hospitals. They represent programs which we believe are good, though we would be the first to recognize that they still leave much to be desired. And they represent programs which any family physician has a right to expect from the state when he refers a patient for medical care to a state hospital. I believe the State is keeping faith, as best it can, with the private practitioner.

Now the patient is ready to leave the hospital and we come right face to face with one of the important hospital-family-physician relationships which has been greatly neglected over the years. I refer to the techniques of keeping the family doctor alert to the progress of the patient and making certain that the patient is returned to his family doctor upon leaving the hospital. We have been trying to work out some efficient procedures in this regard. It is a service which the family doctor should expect. We have been trying to work out some efficient procedures in this regard in one of the state hospitals and serving one of the less active districts in the state. It is something which we will continue to work on and hopefully some day have a plan which can be extended professionally throughout the entire state.

I would ask your indulgence for a very few minutes longer to take a look into one point for the future. I will not take your time to go into the detail of what I visualize as a forward step for the future towards a more comprehensive medical program within the State Mental Hospitals. I will simply state that I hope to live to see the day when the private family physician will have the time to become a part of the public mental hospital, with complete privileges of visiting physician, and will follow his patients during the period of hospitalization. In that capacity I visualize the family physician as caring for his hospitalized patients insofar as the general medical requirements are concerned, in cooperation with the specialists who are on the hospital staff. At a level, the family physician would continue to be the family physician and the general medical consultant for his own patients. In this way, he would maintain closer contact with both the hospital and his patients and the family. I believe that this would enhance the opportunities for better understanding of the patient's illness by all professional persons concerned, and would unquestionably lead to earlier release of many patients from these hospitals—back home to their loved ones and to productive lives. It represents an added program which I would be most happy to work on in connection with any group of recognized private practitioners.

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Young William Rysanek attended the public school near his home—then on to Doctor Deichman's Preparatory School.

Most treasured among the highly prized mementos of those days is the catalog marked:

WILLIAM J. RYSANEK, SR., M.D.

"Maryland Medical College of Baltimore, Maryland 1899–1900." His parents must have read and re-read the pages of that catalog, particularly those headings of: "FEES and REGULATIONS" "LABORATORY FEES" and other items about the "EXTRAS"—hoping they could make it with their limited means.

A few years later, however, these parents must have experienced a joy difficult to describe when they read their son's name among the 92 graduates of the Maryland Medical College on Friday, May 5, 1905 at the Lyceum Theater. He was one of the 18 young men from the State of Maryland to receive the degree of Doctor of Medicine. From here on began a career dedicated to the true purpose of medicine—that of helping to relieve the ills of mankind.

There was another achievement for him in

* Edited by Mrs. William J. Rysanek, Sr. Submitted May 15, 1955 for publication in the MARYLAND STATE MEDICAL JOURNAL.

that year 1905—he was given a place on the Roll of Honor of the Peabody Conservatory of Music as Flutist.

After his graduation, he was assigned to the Franklin Square Hospital, Dispensary Staff, as Chief of Clinic to the Chair of Surgery. It is interesting to note here that Franklin Square Hospital had been only 7 years old when this young physician received the appointment to serve on the Dispensary Staff.

Dr. William J. Rysanek, Sr., who is celebrating his 50th anniversary as a physician, can look back, with much satisfaction, that he too came into the medical profession in that golden age of discovery and achievement at the turn of the century—at the time when Roentgen discovered X-ray; Pierre Curie and Marie Curie were working on the new substance, radium.

Local news made headlines in 1905—two examples are:

During the first week in May 1905 THE SUN published the following news items:

"*Dr. Hurd home from Texas*

Dr. Hurd, Superintendent of the Johns Hopkins Hospital, was very happy over the ratification of the improvements loans on Tuesday, and said—'a sewerage system was absolutely necessary for the future health of Baltimore'. . . ."

"*Cheap Cure for Meningitis*

New York. . . . At the conclusion of the meeting of the Cerebro-Spinal Meningitis Commission, Darlington announced that the commission had concluded that the best treatment for the disease is a thorough system of fresh air. Windows should be open day and night, he said, and plenty of fresh air and sunlight admitted to the sick room. This treatment has been adopted at the Presbyterian Hospital here and elsewhere with the best results. It has been found that when this is done the patient sleeps without administration of an opiate and is comparatively free from pain.

It was also announced that according to tests performed under the direction of the commission no benefit has been derived from the injection of diphtheria antitoxin or any other serum or antitoxin. Experiments along this line, however, have not been abandoned."

From 1905 on to the present time, Dr. William J. Rysanek, Sr. has had medical privileges at the various hospitals in Baltimore, namely:

Dispensary Staff—Franklin Square Hospital (1 year)
Baltimore Eye Nose and Throat Hospital (1 year)
Presbyterian Eye Ear and Throat Hospital (4 years)
Northeastern Health Dispensary (6 years)
West Baltimore General Hospital
Sinai Hospital
Maryland General Hospital
St. Joseph's Hospital
Church Home and Hospital

In addition to his services as a General Practitioner, he had given the greater part of his time to obstetrics, the results of which today bring many happy memories. Some of the outstanding men and women in Baltimore, who are prominent in their professions, he had the privilege of bringing into the world.

Even though he had constant demands on his time, he still had time to devote to outside interests. As flute player in the Orchestra of the Medical and Chirurgical Faculty of Maryland (the only orchestra of Doctors in the country at the time) he participated in all its activities. Still another interest, almost as important as his practice and music, he was—and still is—an ardent baseball fan.

He is a member of the American Medical Association; Baltimore City Medical Society; Southern Medical Association; and the Maryland Academy of Medicine and Surgery.

Born in Baltimore, Maryland—September 28, 1883.

Graduated—Maryland Medical College—May 5, 1905

Dr. and Mrs. William J. Rysanek, Sr. live at 801 N. Kenwood Avenue. They are the parents of:

Dr. William J. Rysanek, Jr. (Duke University School of Medicine)

Dr. Emil J. Rysanek (The Johns Hopkins University School of Medicine)

Mrs. Ruth R. McCleary

Mrs. Joseph M. Cordi

The members of the family of Dr. and Mrs. William J. Rysanek, Sr. honored Dr. Rysanek with a private family dinner on the occasion of his FIFTIETH ANNIVERSARY as a General Practitioner.

801 N. Kenwood Avenue
Baltimore 5, Maryland

PRIVATE SPEECH AND HEARING SERVICES*

JAMES M. LAING

This paper offers answers to questions which the writer has heard asked by physicians. Its purpose is to enlighten, and its motive is to seek more general use of this technical service.

For what is the speech and hearing technician trained?

He is trained to (1) recognize certain early childhood conditions which often lead to later speech and hearing disorders, (2) guide the home in giving the young child maximal opportunity to learn to listen and talk, (3) administer therapeutical guidance to speech and hearing handicapped children and adults, (4) administer speech and hearing tests for patients of family physicians and specialists, and (5) work with rehabilitation professionals in helping victims recover from various types of crippling diseases, accidents, and other tragic experiences.

Is there a national or local directory listing qualified therapists?

Yes. Every autumn of the year, there is published a Directory Supplement of the Journal of Speech and Hearing Disorders. This directory gives the names of all the members of the American Speech and Hearing Association, their certification, places of training, degrees, and address. It lists the members' names alphabetically and geographically. Explanation of the abbreviations are given in the forward part of the directory.

Copies of the Directory Supplement or any other issue of the Journal of Speech and Hearing Disorders may be secured by writing to Dr. George A. Kopp, Business Manager of the Journal of Speech and Hearing Disorders, Speech Clinic, Wayne University, Detroit, Michigan.

How may the services of private speech and hearing therapists be used for the greatest effectiveness?

Prevention needs to be the watchword. Early speech and hearing referral needs to be a frequent prescription.

The validity of these two statements can be indicated best by several case records.

Case A

Jack is a ten year old boy, the second of three siblings. His father, thirty-eight years old, is a steelworker; his mother, thirty-four, is a typist; and his normally talking siblings include a twelve year old sister and a six year old brother.

In the fifth grade, Jack's scholastic rating is good, and his I.Q. is high normal.

Being very talkative, his infantile speech development is very noticeable. Having a negative health record,

* Submitted January 5, 1955 for publication in the Maryland State Medical Journal.

normal hearing (re: pure-tone threshold), normal development history, and normal family surroundings, there is indicated no dramatic etiology.

The only revealing clue from the family history is that Jack never spoke clearly, and during his pre-school years the family had been informed by its physician that Jack would "grow-out-of-it."

It is the experience of qualified speech and hearing therapists that not all pre-school baby-talkers "grow-out-of-it;" but with appropriate home guidance, most of them can be guided out of it before they enter school or soon afterwards.

Case B

Jean is eight years old. Her speech is normal. Being very nervous and jumpy, she was considered inattentive. Because her ten year old brother has cerebral palsy and receives extensive care, it was felt she was striving for special attention. Several times the parents had been told that Jean's inattentiveness was emotional.

After receiving a public school notice that Jean had a hearing loss, her mother brought her to the writer's office for a hearing test. Her pure-tone loss was critical enough to warrant an otologist's special attention; and her speech-reception threshold indicated she was experiencing discomfort in her home and school listening. In hearing discrimination for speech, however, she tested normal. Since her discrimination was normal, there was no way for her parents to have detected the loss indicated by the pure-tone and speech-reception tests.

Jean and her test results subsequently were referred to an otologist.

To the medical and non-medical professionals in the hearing field, it is well known that hearing losses can be determined only by experienced administration of audiometrics. For screening those patients needing otological referral, the family physician has, as one of his aids, the services of those private speech and hearing therapists trained and equipped for doing audiometry.

Case C

Suzan was fourteen years old and in the tenth grade when she was referred as a stutterer. Having a father who had been an Army Warrant Officer, her younger life had been one of constant moving. The mother reported that Suzan began stuttering about the time she was in the third grade and increased when she was about ten years old. She had started school when she was five years old because she insisted upon going to school with an older sibling. Already she had begun to compete with her siblings on an intellectual basis.

Suzan's whole life was one of striving to out-compete with each and all of her siblings. In each and every grade, she was an honor student. Just prior to her referral, her stuttering increased; it increased at a time which coincided with her older sister's winning a nationally outstanding artist's distinction in painting.

Since her case required special psychotherapeutical attention, she was referred to a speech therapist who is associated with the children's psychiatric clinic of an outstanding hospital and who has been trained and qualified for handling psychogenic speech disorders.

This mother too had been informed that Suzan would "outgrow" her stuttering. It is the experience of psychological personnel that stuttering usually is one of several symptoms indicating an anxiety pattern which if reached early can be treated with a minimum of patient-therapist contact.

Case D

Daniel was nine years old at the time his case became active. His voice had a husky quality, and the pitch would have been more appropriate for a man. His hearing was normal (re: pure-tone threshold) and his E. N. T. report was negative.

When he was five years old he had had a tonsillectomy following which his voice became husky and basal. His mother had been told not to worry, that his voice would revert to normal. For a comparatively short time afterwards, tonsillectomized children frequently have husky voice characteristics, but Daniel's persisted. Following one school year of speech (voice) therapy in a Baltimore Public School, his voice sounded more normal in pitch for a boy his age even though much huskiness continued to exist.

Experiences of speech and hearing therapists indicate that guided exercises of the posterior muscles of tonsillectomized children having unusually affected voice qualities will prevent the persistence noted in Daniel's history. Therapists, however, will not administer such exercises without first consulting the child's pediatrician.

Retrospect

In these case records as in many others is stressed the need for prevention. Prevent many of the acute cases normally referred to speech and hearing agencies. Prevent them by referring younger children with only onset characteristics.

Were Jack, for instance, referred when he was four or five years old, he may not have had to be embarrassed at ten with infantile speech. If parents were given prescriptions to have their children's hearing tested once a year or oftener, they would not as likely be caught by surprise as

was Jean's mother. Certainly an early referral to a psychotherapeutically trained speech therapist would have prevented Suzan's problem. In Daniel's case, too, is an example of the need for more preventive techniques and earlier referrals to speech and hearing therapists.

Conclusions

The services of private speech and hearing therapists may be used most efficiently by using the following suggestions:

1. Find the American Speech and Hearing Association certified therapist or therapists in the physician's community or area,
2. Use their services for having questionable patients tested and evaluated for onset characteristics for speech and/or hearing,
3. Prescribe speech and/or hearing therapy for pre-school aged children (four and five years old) with onset characteristics, and
4. Encourage parents to have their children's hearing tested periodically as a prevention step.

204 East 25th Street
Baltimore 18, Maryland

OPEN LETTER TO THE NATION'S DOCTORS FROM S. SLOAN COLT RE MEDICAL EDUCATION WEEK

Since its founding in 1949, the National Fund for Medical Education has concentrated almost wholly on obtaining corporation support for the nation's medical schools. Progress has been slow but steady. Each year has seen an increase over the previous one, both in the number and amounts of company contributions. In 1955 more than 1,500 business firms contributed nearly $1,700,000.

It is, of course, a long way from the $10 million additional annual income required by the schools. But it has shown us what is necessary to win corporation support: a painstaking—and persistent—campaign of education to show business leaders their stake in medical education.

The encouraging part of the picture is the readiness of business leaders to support medical education "once they know the facts." As Colby M. Chester, chairman of the Fund's Committee of American Industry, once said: "If we can get them to sit still long enough to listen, we can get their support."

That is the problem. And it brings to mind the happy thought that nowhere is a businessman more approachable, or more likely to "sit still," than in a discussion with his doctor.

Now I am not suggesting that physicians badger their patients for contributions to the Fund. But I am wondering if doctors cannot be a great ally of the Fund in bringing, in some way, the needs of the medical schools to the attention of the businessmen among their acquaintances. Certainly no one is better qualified to speak authoritatively than doctors. And no one could be more convincing.

Medical Education Week, it seems to me, provides an excellent occasion for beginning such an approach. It will be a period when the needs of the medical schools, as well as the achievements of medical science, will be discussed at meetings businessmen attend and in publications they read. Perhaps then, too, the approach can be followed up from time to time during the year.

Considering the role that the medical sciences have played in safeguarding the people's health, no one has to be timid or reluctant about broaching the subject of continued support for medical education. The testimony of the doctor, coming on the heels of appeals by industry leaders, can do much, in my opinion, to win the businessmen over. Once they are convinced, they are likely to become regular annual contributors to the Fund.

Component Medical Societies

ALLEGANY-GARRETT COUNTY MEDICAL SOCIETY

LESLIE E. DAUGHERTY, M.D.

Journal Representative

Nestled in the Valley at the foot of Will's Mountain and covering 350 acres of land, Allegany County Infirmary cares for Allegany's aged, infirm and mentally sick.

Allegany County Infirmary, Home, Sylvan Retreat

Memorial Hospital Staff Officers

Left to right: Dr. F. T. Cawley, *Secretary* (seated), Dr. F. B. Whitworth, *President* (standing).

The Infirmary was established in 1949 and the bed capacity is 95, with a daily average census of 95 and houses bed patients only.

The County Home bed capacity is 48, with a daily census of 40 ambulatory patients. The Home was established in 1850.

The Sylvan Retreat received its license in 1889 and has a bed capacity of 90, with an average census of 89 patients. Here the mildly insane are cared for, until or unless, it is necessary to remove them to the Springfield State Hospital. It also serves as a detention home for girls and boys, while undergoing investigation by the Courts.

Dr. James E. McLean, of Cumberland, is the County Physician.

Dr. Harold W. Eliason, Member, State Advisory Council on Hospital Construction (seated).

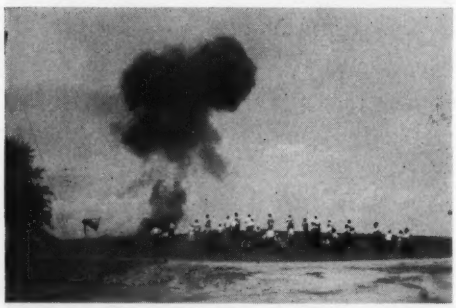
Cumberland Memorial Hospital Staff Officers—1956

The Memorial Hospital staff organization for 1956, includes Dr. Fuller B. Whitworth, President; Dr. Wylie Faw, Vice-President and Dr. Frank T. Cawley, Secretary-Treasurer.

The staff consists of 63 physicians and surgeons and meets the second Friday of every month.

The average daily census for Memorial Hospital, is 235.

Casualties Cared for by Lay Personnel.



Newer Bombs Wipe Everything Out in a Seven Mile Area.

Fire Fighting and Salvaging Those Not Killed Outright Important.

Dr. Eliason Named Member of State Hospital Planning Board

Dr. H. W. Eliason, of Cumberland, has been appointed by Governor Theodore R. McKeldin, as a member of the State Advisory Council on Hospital Construction.

The Council was established in 1947 and is composed of eleven members, appointed by the Governor for three-year terms. The Council is to consult and advise with the Board of Health in the administration of a state plan of hospital construction, under terms of the Hill-Burton Act.

Dr. Eliason specializes in pediatrics and is Chief of Pediatrics at the Cumberland Memorial Hospital. He has practiced in Cumberland since 1928 and graduated from the University of Maryland in 1927 and interned for one year at Mercy Hospital. He is on the Board of Health for the Cumberland City Health Department since 1954 and is married and has one married daughter.

Allegany County Prepares for All Out War by Civil Defense

It may never come here, but Allegany County is getting ready at full speed for any emergency; what, with new industries making Cumberland more than ever a target for actual bombing.

A new multimillion dollar industrial plant that will make bomber equipment, if and when war comes, has located in Cumberland.

Increased acceleration in Civil Defense training, has become necessary and under the direction of Dr. Leo H. Ley, Jr., Assistant Medical Director, for Civil Defense in Allegany County, first-aid teams of Casualty Clearing Stations, #1 and #2, with Drs. Clay Durrett and Overton G. Himmelwright, Chief physicians, have started actual demolition casualty care and are going throughout the County, training teams for any catastrophic conflagration.

Dr. Leslie E. Daugherty is Medical Director for Civil Defense in Allegany County.

BALTIMORE CITY MEDICAL SOCIETY

CONRAD ACTON, M.D.

Journal Representative

The February session of the Executive Board spread over two long, active meetings on 28 February and 6 March. This was due largely to the very intense interest shown by all its members in Physicians Defense as it might apply to the younger members of the profession and hospital resident staffs. Individuals concerned by a court action last year accepted the invitation to discuss the situation in that case: How it started; what made suspicion possible; how it developed; and all the circumstances surrounding it.

The Board's position was that although resident staffs may or may not be members of the City Society individually yet the Society has a responsibility as the representative of organized medicine. In particular it has a duty toward young physicians, to see that rights are safeguarded, privileges maintained, and avoidable indignities abated.

Mr. G. C. A. Anderson, counsel retained by the Society, assisted in the interrogation. He later took occasion to amplify the changing picture of medical malpractice. Emphasis is now being put in the Courts on "involuntary negligence" and awards are for ever larger amounts if a doctor is found guilty. This he says is particularly true in England. Also in California, Texas, Tennessee, and the District of Columbia; and he referred the Board to an article from which he quoted in the "Insurance Counsel Journal" for January 1956, page 23. The increasing number and size of the claims has caused insurance firms to discontinue malpractice coverage; others have increased premiums.

Our "Physicians Defense," involving professional but not financial support, shares in the over all problem and burden of increased litigation. Malpractice is different from the usual medical expert testifying. In malpractice it is necessary for medical witnesses to hear all the evidence in the particular case at trial. Unless they hear *all the evidence in the particular case* they are not legally competent to testify as experts in that particular case. Mr. Anderson stated that physicians called on to assist in the defense of other physicians were protesting that they could not spare the requisite two or three days from their practices. He urged the Executive Board to encourage physicians to stand by each other in time of need. He advised us bluntly that physicians will be taken advantage of unless they fight the growing malpractice racket, and when they fight they have got to give it all they've got or be beaten.

Dr. Charles R. Goldsborough, Chairman of the Legislative Committee, presented a concise digest of the status of the Bricker Amendment and the doings of the International Labor Organization as they bear on the practice of medicine. He admitted that he had been quite indifferent to the hue and cry concerning these two matters until, as Chairman of his Committee, he started scanning the data. Now he is quite alarmed at the peril they pose for our Country and way of life. He and his Committee urge thoroughgoing support of the Bricker Amendment and complete withdrawal from the stacked International Labor Organization. He hopes all members of the City Society will read and digest the literature sent to them and take positive action as their judgment indicates.

A letter from the President of the Woman's Auxiliary to the Baltimore City Medical Society was read at the second meeting of the Board on 6 March. Taking a cue from other Auxiliaries, ours is donating $50 to the AMA Educational Fund instead of spending the same amount for buttonholing us with red carnations. The Board felt that this was certainly a more practical form of remembrance.

Insurance again came up in two directions. Should the permanent disability insurance now effective for five years be extended to a ten year coverage—at an increase in premium—for those desiring it? Also, could indemnity insurance be assigned by the patient to the physician in advance. This was to prevent the patient failing to pay later on receipt of the whole amount. Since this concerns one particular company chiefly, the Insurance Carrier was interrogated. The Company wrote that such assignments, in proper form would be honored by the insurance company, but that the Forms for reporting could not be altered to include it. Possibly for fear of labor contract repercussions and renegotiations??

On Friday, 2 March, the regular monthly meeting was well attended. President Dr. Grant Ward introduced the guests of the month, Dr. Paul Stonesifer, *President*, and Dr. Charles W. Stewart, Jr., *Vice-President*, of the Harford County Medical Society. He then called on Mr. G. C. A. Anderson who very forcefully presented to the large meeting the necessity for member attendance at Physicians Defense trials and the basic difference from other medical testimony, as previously outlined to the Executive Board.

Dr. Charles R. Goldsborough gave his report on the Bricker Amendment, International Labor Organization, and HR 7225. Obviously hampered by time limitation he was well received by the audience.

Dr. Robert Kimberly, Treasurer, reminded us of the new "dread disease" type coverage, $300 deductible, as an extension of Blue Cross-Blue Shield in the physician's personal and family protection.

Response has been slow. He told us that fifty per cent of the membership must join to effect a blanketing in of all applicants. If less than that many apply, selection will be on the basis of usual actuarial criteria.

A symposium on "Uses and Abuses of Antibiotics" was the scientific portion of the meeting and was moderated by Dr. George S. Mirick, Physician-in-Chief, Baltimore City Hospitals. He outlined the broad divisions adopted by the participants and introduced Dr. Theodore E. Woodward, Physician-in-Chief, University Hospital, who had distributed a "Tentative Guide for Chemotherapy of Specific Infectious Diseases." He proposed the theoretical requirements of an ideal antibiotic and discussed the available ones in relation to the ideal. He discussed the changing attitude regarding prophylaxis of infections with antibiotics. He noted that in measles and in intestinal surgery it seemed to be proving ineffective.

Doctor Mirick discussed the problem of resistant infections. He finds with ever widening experience and deepening statistical tables that body factors are increasingly important in resistance to bacterial invasion. The nature of the underlying disease makes the diagnosis paramount in resistant infections. He assented that he saw little benefit to be gained from prophylactic use of antibiotics for organisms, can lie metabolically dormant for years, and antibiotics kill only multiplying organisms. His view was that it was better to treat the infections as they arise. In *resistant* infections the diagnosis, anatomy, and biology must first be understood to make chemotherapy effective.

Dr. Ivan L. Bennett, Jr., Physician, Johns Hopkins Hospital, presented the problem of antibiotic toxicity. He had beautiful slides illustrating the cutaneous and mucosal reactions of allergy to antibiotics. He showed how drug fever is disconcerting to the physician and expensive to the patient when recognized late. In discussing superinfections he disclosed a study of membranous enterocolitis in chinchillas apparently due to an antibiotic and pathologically identical with similar lesions in humans.

Coffee, cocoa, and doughnuts were provided, at the close of the meeting, by the Woman's Auxiliary, graciously dispensed by Mrs. William Lynn and Mrs. Raymond Rangle, co-chairmen of their Hospitality Committee.

BALTIMORE COUNTY MEDICAL ASSOCIATION

DONALD L. SOMERVILLE, M.D.

Journal Representative

New Emergency Medical Service

The physicians of the Reisterstown area announce the formation of the new emergency service to provide complete coverage for their patients at all times. The schedule of duty for night and weekends has been posted in the local fire departments, police stations, and pharmacies. It is the sincere hope of the Baltimore County Medical Association that every patient be able to get a physician in an emergency.

FREDERICK COUNTY MEDICAL SOCIETY

LOUIS R. SCHOOLMAN, M.D.

Journal Representative

The regular February meeting was held at the Frederick Hotel on the twenty-first. The speaker of the evening was Mr. Lloyd Ambrosen, superintendent of the Maryland School of the Deaf. His talk on the Education of the Deaf Child was informative and thought provoking.

Dr. Robert Pilgram, local surgeon, after performing the priestly rites on the morning of February 13 became the sacrificial victim the same evening. He lay on the table upon which he had so often leaned and underwent an appendectomy.

Hospital Events

Three interesting cases were presented at the monthly staff meeting. Drs. Powell and Heldrich described the onset of tuberculous meningitis in an eight month old infant while the child was being treated with Streptomycin. Drs. Lea and Harp discussed a case of severe G.I. bleeding caused by a leiomyoma of the jejunum. Dr. Guest presented the third case, which was that of a twenty-nine day old premature who died of peritonitis secondary to a ruptured appendix.

The medical and pediatrics department had a

joint meeting on the 24th. Dr. Schoolman presented a case of hypersensitivity simulating anterior poliomyelitis.

The C.P.C. was that of a two year old child with mucovisidosis who died from an overwhelming hemolytic staphylococcus aureus bronchitis and bronchopneumonia.

MONTGOMERY COUNTY MEDICAL SOCIETY

JAMES P. McCARRICK, M.D.

Journal Representative

The monthly dinner meeting of the Society was enjoyed at the Norbeck Country Club. Following the dinner a panel discussion on the practical uses of radioisotopes was well received. The panelists were, Dr. Murray Copeland, Professor of Oncology at Georgetown University Medical School; Dr. B. J. Duffy, Jr., of the Georgetown Radioisotope Laboratory and Captain King of the Bethesda Naval Hospital.

The Society wishes to welcome the following new members:

Active Membership

Dr. Gary Owen Morris
7942 Wisconsin Avenue
Bethesda, Maryland

Affiliate Membership

Dr. David Franklin Hodge
4630 Montgomery Avenue
Bethesda, Maryland

U. S. AID PROPOSED TO IMPROVE HEALTH OF LOW-INCOME FAMILIES

The AMA Washington Letter, No. 84–54

After intensive hearings, a Senate subcommittee recommends that the federal government take special action to improve the health of the nation's low-income families. The subcommittee, under chairmanship of Senator Sparkman (D., Ala.) made its report January 2 to the Joint Committee on the Economic Report. Among its proposals:

1. That Congress consider legislation to cover the risks of temporary and permanent disability, but that first a study be made to determine the desirability and feasibility of dovetailing such programs with workmen's compensation acts of the states. The report quotes Senator Flanders (R., Vt.) as saying, "This undertaking must be approached with great caution. Many insurance companies have had to discontinue disability benefits owing to the difficulty of defining 'disability,' whether temporary or permanent, in any given case."

The Senate Finance Committee, of which Senator Flanders is a member, now has before it a House-passed bill to establish a system of cash payments for disability under the Federal Social Security program; it would not be related to workmen's compensation or other state benefit plans. A number of national organizations, including the AMA, are opposed to this legislation, maintaining that the whole social security system should be thoroughly and objectively reviewed before such a far-reaching new program is enacted.

2. That the Federal Government, cooperating with states and private groups, develop a comprehensive health program that will provide (a) stimulation of adequate care for rural families, (b) reduction in the cost of catastrophic health insurance, possibly with U. S. paying part or all the premium for low-income families, and (c) possible U. S. help so low-income families can buy basic health insurance protection.

The subcommittee also recommends several broad steps to liberalize present public assistance grant-in-aid programs and child welfare services.

Necrology*

Jonas Stein Friedenwald, M.D.

1897–1955

Jonas Stein Friedenwald was born in Baltimore on June 1, 1897. He was the son of Dr. Harry Friedenwald, a distinguished ophthalmologist, scholar and historian. He was the grandson of Dr. Aaron Friedenwald whose name is eminent in Maryland medical annals. Thus by birth he was a member of a proud and aristocratic Jewish family, one dedicated to science and scholarship, with a high sense of pride in the ancient traditions of their race and a stalwart sense of personal honor and integrity. This was Jonas Friedenwald's rich heritage, and one he not only upheld, but advanced.

He was educated in The Johns Hopkins University and received the degree of Doctor of Medicine there in 1920. He served one year as house officer in the medical service of The Johns Hopkins Hospital. Thereafter he studied ophthalmic pathology under Dr. Frederick Verhoeff at Harvard University where he received the degree of Master of Arts. From 1922–23 he studied clinical ophthalmology under Dr. George E. de Schweinitz in Philadelphia and returned to Baltimore in 1923 to begin practice of ophthalmology with his father. In the light of present standards this may at first glance appear as scant preparation for either research or practice. But such was Dr. Jonas Friedenwald's amazing brilliance of mind and his capacity for assimilation that he was in fact an extraordinarily well-trained man when he returned to Baltimore. From 1923 up to his untimely death in 1955, his career was one of brilliant accomplishment which has few equals in American ophthalmology.

In 1923, he was appointed to the pathology service of the Johns Hopkins Hospital under Dr. George MacCollum. Here he was in charge of ophthalmic pathology. When the Wilmer Institute was founded in 1925, he was appointed to the ophthalmology staff and was made responsible for its pathology laboratory and for instruction in ophthalmic pathology. Thereafter, he was rapidly promoted through the various academic grades and was finally appointed Associate Professor in 1931, which position he held at the time of his death. Due to the fixed assignment of titles in the various services of the Johns Hopkins University School of Medicine, he could not be appointed to a full professorship in ophthalmic pathology. However, there never has been a member of the Johns Hopkins medical faculty who would have graced a full professorial title with more distinction. Throughout the last twenty years of his life he was in full charge not only of the department of pathology of the Wilmer Institute, but also of the lion's share of its research activities.

The story of Dr. Friedenwald's research activities is amazing. It ranges from ophthalmic pathology to physiological optics, to experimental physiology, to experimental pathology, and on through intricate and highly specialized investigations in biochemistry and histochemistry. In each of these fields he became not only a distinguished contributor, but also a leader. Perhaps his most notable investigations were on the pathogenesis of acute and chronic glaucoma, studies which made him world-famous.

His honors were many. Among the most notable were the awards of the medal for distinction in ophthalmology by the American Ophthalmological Society in 1951, the ophthalmic research medal by the American Medical Association in 1935, the Donders Medal by the Dutch Ophthalmological Society in 1952, and the first Proctor Award of the Association for Research in Ophthalmology in 1948. He served for a number of years as chairman of the Committee on Tonometry, a project sponsored by the four national ophthalmological societies, and was responsible not only for the present standardization of tonometers, but also for a great number of improvements and refinements in practical tonometry and the clinical measurement of aqueous outflow. He was one of the editors of the A.M.A. Archives of Ophthalmology and the Journal of Histochemistry and Cytochemistry. His influence on younger men was immense. Such was his national and international fame that students came not only from

* Memoir Committee: A. S. Chalfant, M.D., *Chairman*, John F. Hogan, M.D. and Robert H. Riley, M.D.

America, but from many foreign countries to study under him and learn his research techniques.

In addition to his fundamental investigations into the genesis of disease and many contributions to ophthalmic science, Dr. Friedenwald carried on a private practice and was pre-eminent both as a diagnostician and clinician. Such was his energy and versatility that he could not content himself with this combination of clinical work and scientific investigation. He explored and became profoundly interested in many legal, social, and cultural problems. An example of his wide interest in esoteric problems is that at one time he actually studied and mastered a textbook on the basic problems of common law in order that he might clearly understand and argue intelligently on certain questions under dispute! His interests extended to music and to art, and like many other distinguished men, he made an avocation of painting.

Among the most outstanding of his varied activities was his intense interest in the problems of his own people—in Zionism and in Israel. He was a member of the Council of Hadassah Hospital and Medical School in Israel, and made two lengthy visits to that university. On one of these he actually delivered a course of lectures in Hebrew—which language he studied for months for this one and only purpose.

The stature of Jonas Friedenwald was such that it is difficult to express its full magnitude in this limited space. He was a great teacher and investigator, an eminent clinician, a scientist of the widest interest and attainment, a scholar of the arts and humanities, and a citizen of the highest eminence. With his death American and world ophthalmology lost one of its most brilliant investigators. The city of Baltimore and the State of Maryland lost one of their most eminent citizens. The Medical and Chirurgical Faculty lost one of its most distinguished members.

ALAN C. WOODS, M.D.

Milton L. Solomon, M.D.

1903–1956

It has been said that no one has had a full life unless he "died in harness," with much of his beloved work undone.

Dr. Milton L. Solomon finished one of his very full days of activity in his office and died in his easy chair a very short while after he returned home. Thus ended suddenly on February 14, 1956, the useful career of a beloved family physician at the age of 52.

He was born in Brooklyn, New York in 1903, graduated from the College of the City of New York in 1925, graduated in high esteem from the University of Maryland School of Medicine in 1929; and then served an internship and assistant medical residency in Kings County Hospital, New York. While at this Hospital he married a Baltimore girl. He elected to return to Baltimore where he cast his lot and served with the great populace in the eastern part of the City; and this populace loved him. In this community he established the modern type of practice of internal medicine which was highly ethical, enduring as well as inspiring to both doctors and patients. Conscientious to the extreme he "gave his all" to his patients until his last minutes on this earth.

In spite of a busy practice he found time and interest during many of his early years to engage in research in the field of endocrinology with Dr. Eduard Uhlenhuth at the University of Maryland School of Medicine.

Dr. Solomon is survived by his wife, Lillian, and two sons—the elder, Harvey, is now a student in the University of Maryland School of Medicine, and the younger, Gene, is a student in Education at the University of Maryland, College Park, Md.

CALVIN HYMAN, M.D.

Library

"Books shall be thy companions; bookcases and shelves, thy pleasure-nooks and gardens." *ibn Tibbon*

LIBRARY CHATTER

MARY EMILY BERGE

We are not sure whether to be glad or sorry to say that the final regular volume of the Index Catalogue of the Surgeon General's Office (Armed Forces Medical Library) is now available for use in the Library. We are glad to have it, for obvious reasons, but sad that it *is* the final volume. This volume, which is number 11 of the fourth series, completes the letter "M" and brings to a close, at least in the same format, this monumental medical bibliography. William Henry Welch once called the Index Catalog America's most important contribution to medicine. The reason for ceasing publication is, of course, the enormous amount of literature on the medical sciences. The Index Catalog simply could not keep up with it. A supplementary series is planned to cover monographic, but not periodical, material up to 1950. The new quinquennial cumulation (1950–1954) of the Armed Forces Medical Library is already available for use in the Faculty Library. With the "Current List," indexing periodicals, in constant use, the major part of the world's output of medical literature is covered.

Our stack assistant, Ella Chatt, has resigned to accept a better position elsewhere. During her five years at the Faculty, Ella made an extremely valuable contribution to the work of the library and we were sorry to lose her. We wish her success in her new position.

YELLOW FEVER CONTINUES NORTHWARD, DR. SOPER REPORTS

The AMA Washington Letter, No. 84–60

Back from a three-month round-the-world health survey, Dr. Fred L. Soper, head of the Pan American Sanitary Bureau, has both somber and heartening news. He warns that after a lapse of 18 months, yellow fever in monkeys has resumed its slow progress northward and is now near the northern border of Honduras. This is only 75 miles from the southern edge of the area of the aedes aegypti mosquito which is the urban vector of yellow fever in the U. S. Adds Dr. Soper: there are no natural barriers in this marrowing gap between Honduras and Mexico.

But generally, Dr. Soper notes an improvement in national health services particularly in the Far East, which he attributes to the World Health Organization. Other reasons for the improved situation: absence of war, improved nutrition, better working conditions, decrease in other diseases, especially malaria, and improved tuberculosis therapy. Malaria, however, continues to impose a great burden on health services throughout the Far East, he said, adding: "To eradicate malaria . . . will call for action on a world scale. It will cost hundreds of millions of dollars.

Health Departments

BALTIMORE CITY HEALTH DEPARTMENT

Paralytic Poliomyelitis Experience in Baltimore

1950–1954

As a result of the concentration of early inoculation efforts in 1954 and 1955 with the new poliomyelitis vaccine among children 6–7 years old, the impression seems to have grown that children in the school ages are the individuals who are at the highest risk of attack by poliomyelitis. Recently, there has been some reticence shown by mothers visiting the Health Department Well Baby Clinics to give their assent to the poliomyelitis inoculation of their children in the pre-school ages, 1–5 years. In order to clarify this matter, Dr. Matthew Tayback, Director of the City Health Department's Statistical Section, has studied the paralytic poliomyelitis experience for Baltimore City during the five year period 1950–1954 during which there were 405 paralytic cases reported. Some of his findings are presented as follows:

"The age specific rates of the incidence of paralytic poliomyelitis for separate years of age are shown below according to race.

Annual Average Incidence Rates for Paralytic Poliomyelitis By Age and Race

Baltimore City, 1950–1954

Age (Years)	Rates Per 100,000 Population	
	White	Nonwhite
Under 1	17.3	8.3
1	50.5	26.9
2	34.2	37.5
3	57.6	26.7
4	39.0	15.0
5	43.3	19.8
6	39.9	19.8
7	34.6	9.1
8	24.2	4.7
9	25.1	4.9
10–14	18.6	2.2
15–19	9.6	1.2
20–24	7.4	2.3
25 and Over	1.7	0.4

The children in Baltimore City who are most at risk of paralytic poliomyelitis are in the pre-school ages, i.e. under 6 years of age. Among white children, rates of paralytic poliomyelitis in the school ages 6–14 remain at levels which would suggest the necessity for the earliest possible inoculation of this group. It is of extreme interest that the incidence of paralytic poliomyelitis among Negroes is, with the single exception of the two year olds, at least 50 per cent lower at all age levels than the comparable white group. There is little question but that the prime emphasis of an inoculation program among Negro children should be directed towards individuals below the age of six years."

Family physicians and pediatricians will be interested in the facts shown above. They appear to indicate that available vaccine should be employed to the fullest extent to protect children in the pre-school ages, one to five years old, inclusive.

Huntington Williams, M.D.

Commissioner of Health

ADMISSION POLICY OF CHRONIC DISEASE HOSPITALS

In a discussion recently with Dr. A. S. Dowling, Medical Director of the Chronic Disease Hospitals, admission policies of these institutions were reviewed. Dr. Dowling offered the following comments.

The State of Maryland is presently operating two hospitals for patients with chronic disease. Located in Salisbury and in Baltimore City, they have a combined capacity of approximately 450 beds. Facilities are under construction which will provide approximately 300 beds in Hagerstown and 250 additional beds in Baltimore, but it will be many months before these are available.

For several years applications for care have been greatly in excess of available beds. It seems therefore desirable to define, more clearly, the types of patients presently being accepted by these hospitals. "Acceptable" or medically eligible applicants are classified by the Hospital Admissions Board as follows:

Class I:

(a) These patients give *medical evidence of rehabilitation potential.*

(b) For administrative reasons *patients occupying state-aided beds* in general hospitals are placed in Class I provided they are otherwise acceptable.

Class II:

Patients who require hospitalization to establish whether or not there is a rehabilitation potential. These patients are accepted with the understanding that prompt discharge will be accomplished if a rehabilitation potential is found lacking.

Class III:

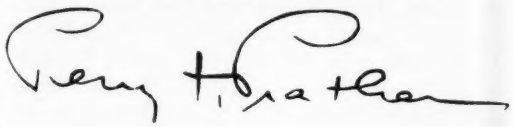
Patients with terminal conditions requiring medical and hospital care beyond that available in the home or nursing home.

Class IV:

Readmissions: Patients previously discharged from the chronic disease hospital with the understanding that re-admission would be accomplished with a minimum of delay, if and when their condition progressed to the extent that adequate care was no longer possible outside a hospital.

It should be pointed out that the foregoing is a *classification* of patients—not a priority listing. Insofar as possible, priority in terms of hospital admission is based upon *medical* need, order of application, etc., but availability of a suitable bed must enter into the final decision as an important element in any single case.

When more beds become available, it is earnestly hoped that prompt admission may become the rule rather than the exception. This will reduce hardship on the family and patient, relieve the general hospital of long term care in many instances and assure a more prompt initiation of those corrective measures which the chronic disease hospital provides.



Director

$401,960 U. S. AWARDS IN GRANTS FOR HOSPITAL RESEARCH

The AMA Washington Letter, No. 84–54

Public Health Service has awarded $401,960 in grants for hospital research, the first allocations from a $1,200,000 fund appropriated in the last session of Congress. Eligible for the grants are states, counties and communities, universities, hospitals, and other nonprofit institutions. Work must be directed toward developing new information on the use of hospital services, facilities, and resources. Initial recipients and amount of grants:

Association of University Programs in Hospital Administration to develop research procedures in hospital and related fields, $75,000; American Hospital Association to study hospital planning and license laws, $71,487; Catholic Hospital Association, for two projects in hospital operations, $10,100; American Pharmaceutical Association, for audit of hospital pharmaceutical services, $36,000; University of Arkansas, for a study of function of general duty nurse in record-keeping, $14,850; Mississippi State College for study of hospital and its community relations, $16,500; New York State University Research Foundation for study of impact of teaching and research on hospital operating costs, $10,870; and American Psychiatric Association for study of mental hospital architectural needs, $66,534.

STATE OF MARYLAND DEPARTMENT OF HEALTH

MONTHLY COMMUNICABLE DISEASE REPORT

Case Reports Received during 4-week Period, March 30–April 26, 1956

	CHICKENPOX	DIPHTHERIA	GERMAN MEASLES	HEPATITIS, INFECT.	MEASLES	MENINGITIS, MENINGOCOCCUS	MUMPS	POLIOMYELITIS, PARALYTIC	POLIOMYELITIS, NON-PARALYTIC	ROCKY MT. SPOTTED FEVER	STREP. SORE THROAT INCL. SCARLET FEVER	TYPHOID FEVER	UNDULANT FEVER	WHOOPING COUGH	TUBERCULOSIS, RESPIRATORY	SYPHILIS, PRIMARY AND SECONDARY	GONORRHEA	OTHER DISEASES	DEATHS: Influenza and pneumonia
Total, 4 weeks																			
Local areas																			
Baltimore County	89	—	39	—	241	1	81	—	—	—	17	—	—	2	15	1	1	m-1	8
Anne Arundel	21	—	5	1	108	—	20	—	—	—	1	—	—	—	4	—	3	m-1	4
Howard	—	—	—	—	8	—	—	—	—	—	—	1	—	—	1	—	—	—	1
Harford	1	—	2	—	8	—	3	—	—	—	—	—	—	—	14	—	1	—	1
Carroll	2	—	—	—	17	—	2	—	—	—	—	—	—	—	1	—	—	—	1
Frederick	8	—	28	—	30	—	—	—	—	—	9	—	—	—	—	—	2	—	—
Washington	6	—	—	—	2	—	—	—	—	—	—	—	—	—	5	2	1	—	2
Allegany	—	—	—	—	45	—	—	—	—	—	2	—	—	1	4	—	1	—	1
Garrett	—	—	—	—	2	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Montgomery	45	—	6	—	188	—	30	—	—	—	15	—	—	—	10	—	—	h-1	7
Prince George's	21	—	2	—	107	2	17	—	—	—	13	—	—	—	7	1	—	—	2
Calvert	—	—	—	—	3	—	2	—	—	—	—	—	—	—	—	—	—	—	—
Charles	—	—	—	—	3	—	1	—	—	—	—	—	—	—	2	—	—	—	—
Saint Mary's	10	—	—	—	86	1	—	—	—	—	2	—	—	—	—	—	—	—	2
Cecil	—	—	1	—	8	2	11	—	—	—	4	—	—	—	6	—	3	—	3
Kent	1	—	—	—	4	—	3	—	—	—	—	—	—	—	—	1	—	—	—
Queen Anne's	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1
Caroline	—	—	—	—	—	—	1	—	—	—	1	—	—	—	—	—	1	—	—
Talbot	—	—	1	—	5	—	—	—	—	—	—	—	—	—	—	—	3	—	—
Dorchester	2	—	—	—	19	—	8	—	—	—	—	—	—	—	2	—	2	—	1
Wicomico	—	—	—	1	1	—	—	—	—	—	2	1	—	1	3	—	1	—	2
Worcester	—	—	—	—	—	—	4	—	—	—	—	—	—	6	2	—	—	—	1
Somerset	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1	—	—	—	1
Total Counties	206	0	84	2	885	6	183	0	0	0	66	2	0	10	77	5	19		39
Baltimore City	203	0	108	8	517	3	211	0	0	0	37	0	0	3	93	15	460	t-2	27
State																			
Mar. 30–Apr. 26, '56	409	0	192	10	1402	9	394	0	0	0	103	2	0	13	170	20	479		66
Same period 1955	407	0	94	31	293	4	272	1	0	0	321	0	0	26	161	20	556		43
5-year median	559	1	168	44	995	8	320	2		0	252	2	2	29	217	15	486		64
Cumulative totals																			
State																			
Year 1956 to date	1698	0	450	50	7605	26	1428	1	0	0	447	3	0	64	702	102	2007		331
Same period 1955	1588	1	228	145	749	13	917	3	1	0	1802	0	0	138	637	55	2244		288
5-year median	2128	8	357	169	3215	35	1101	7		0	989	7	6	163	781	75	2178		293

h = Hansen's disease.
m = Meningitis, other than meningococcus.
t = Tetanus.

Blue Cross - Blue Shield

BLUE CROSS IN ONE GENERATION

R. H. DABNEY*

Today, more than 50 million people in North America have Blue Cross. These subscribers, enrolled through 86 Blue Cross Plans, budget for hospital care in advance, paying regular amounts through prepayment in much the same way as they finance other expenditures in the family budget. In 1955, these Blue Cross subscribers received $885 million in hospital care benefits.

Most Blue Cross membership is in employed groups where subscription charges are collected by payroll deduction, and where, in many cases, the firm participates in the cost of the protection. Although there is no one factor basic to the success of Blue Cross, it is an acknowledged fact today that union-management negotiations in the post-war period contributed largely to the significant growth in membership in voluntary prepayment plans.

As Blue Cross has acquired more and more experience, important extensions have been made to provide broader benefits, not only to subscribers in groups, but to those who in the early stages of the movement were unable to join. Here in Maryland, for example, there is a non-group membership program which in less than two years has grown to include some 10,000 people.

The group programs, too, have advanced far beyond the original basic Blue Cross programs offering, say 21 days, of hospital care. In Maryland, some 18% of the total Blue Cross membership is enrolled through what we call "special contracts" providing 70 or 120 days of hospital care, and other benefit extensions beyond the scope of the basic standard program.

Blue Cross is now just entering its second generation. The impact for hospitals and subscribers alike is implicit in the fact that now about one person in three has membership. This indicates the widespread public acceptance of Blue Cross, but this large membership is all the more significant when you understand the fundamental concepts which from the very beginning have guided the Blue Cross Plans.

The common goal for all Blue Cross Plans has always been to make hospital care available to the greatest number of people in the community at the least possible cost, with benefits that are realistic in terms of hospital service itself.

In 1929, when the depression was imminent, a group of schoolteachers in Texas approached a hospital administrator to work out some practical solution to their problems. For the schoolteachers, it was essential for them to find some way to pay for hospital care. For hospitals, it was no less imperative that some means be developed to finance their services to the community. From this joint need the Blue Cross Idea was established.

The idea worked. It caught the imagination of other people with similar problems in other communities, and before long Blue Cross Plans began to spring up across the nation, different in some features depending upon local conditions, but all basically the same in objectives and organization. Such was the popular appeal of Blue Cross that in 1934, just five years after the idea began, the American Hospital Association gave its official approval and support to Blue Cross and established certain standards which today still guide Blue Cross Plans in their local operations.

To earn the right to use the Blue Cross emblem, each Blue Cross Plan in the nation must each year submit records of its operations to the American Hospital Association for approval. The general standards for approval include hospital representation and responsibility, sound financial operations, non-profit sponsorship and control, medical and lay representation, and service benefits—as opposed to cash allowances—for the basic semi-private services.

Blue Cross has been called the "financing arm" of the general hospitals, which means that Blue Cross, in providing benefits to subscribers, likewise organizes funds from people in the community to finance hospital care. Last year, for example, Maryland Blue Cross paid $14,842,778 in hospital care benefits, and this record amount brings total pay-

* Executive Director, Maryland Hospital Service, Inc., Maryland Medical Service, Inc.

ments to almost $82 million. The record is much the same in other communities in the nation.

Problems lie ahead. With economic and social changes in the last decade, along with modern advances in hospital methods and medical science, Blue Cross will have even greater opportunities to adapt its basic characteristics to the growing needs of the public. It is estimated that in 1956 one person in seven will be hospitalized, and that one family in three will have a hospital bill to pay.

Blue Cross has the experience to meet the expanding needs of people in the community, and the support from hospitals and from the medical profession to find solutions to the problems that will confront Blue Cross in the future.

SENATE SUBCOMMITTEE CONSIDERS COMMISSIONS FOR OSTEOPATHS

The AMA Washington Letter, No. 84–60

After a one-day hearing at which representatives of the medical profession, osteopathy and the Department of Defense were heard, a Senate Armed Services subcommittee is considering legislation authorizing the Armed Forces to commission osteopaths. The bill (H.R. 483) passed the House last session. Chairman of the subcommittee is Senator Stuart Symington (D-Mo.).

While the Defense Department favors the bill, the surgeons general of Army, Navy and Air Force oppose it. Dr. Edward H. Cushing, deputy assistant secretary for health and medical matters, supported the bill, but told the subcommittee that the heads of the three medical departments "have certain reservations." The surgeons general probably will be heard late next week. Dr. Cushing said the present policy is to defer osteopaths.

Dr. James R. McVay, a Trustee of the AMA, pointed out that unlike a civilian, the man in the armed forces is not free to select the type of medical care he desires, but must accept that furnished, and "up to this point . . . the care provided has been of the highest quality." He declared:

". . . The appointment of osteopaths as medical officers will endanger the health and welfare of our military personnel, will contribute to the demoralization of our career medical services, will endanger the accreditation of residency and internship training programs in military hospitals, and will unnecessarily hinder the utilization of civilian consultants and other civilian physicians by the armed services."

Dr. Daniel F. Hanley, executive secretary of the Maine Medical Association, after first outlining the progress of medical science in the last 80 years, said: "Medicine and osteopathy are different disciplines. . . Legislating them to be equal can only bring chaos. . . With time and cooperative effort the differences between medicine and osteopathy will be resolved. But I sincerely believe that the Armed Forces is not the forum in which to find the answer."

Spokesmen for osteopathy cited various state court decisions and parts of the AMA report on osteopathy (June, 1955) as evidence that osteopaths are qualified to care for patients. They indicated that about 4,000 osteopaths would be available for service under the doctor draft. Witnesses for the osteopaths were J. S. Denslow of the Kirksville College of Osteopathy, secretary of the American Association of Osteopathic Colleges, and James O. Watson of Doctors (osteopathic) Hospital in Columbus, Ohio and a member of the Ohio State Medical Board, both doctors of osteopathy; and L. L. Gourley of Washington, D. C., counsel for the American Osteopathic Association.

Ancillary News

NURSING SECTION

M. RUTH MOUBRAY, R.N., *Executive Secretary,*
Maryland State Nurses Association

REFRESHER COURSE FOR NURSES

The Hospital for the Women of Maryland has had more than forty registered nurses complete refresher courses in nursing since the inception of the program in September 1954 following discontinuance of its three-year diploma program. Fifteen of these nurses are now employed at Women's. Most of the others have become engaged in some field of nursing elsewhere.

The six weeks' course is conducted by a full-time instructor. It is designed to prepare nurses who have been inactive to resume the practice of nursing. Special emphasis is given to new medications and treatments in the care of the sick. Formal instruction is given three days a week for a total of eighteen hours a week. There is no charge for the course.

The opportunity offered at Women's has particular value to nurses in that it provides a sense of security for them as they reenter the field of nursing under careful supervision. Nurses desiring such experience may be referred to Miss Evelyn M. Hulse, Director of Nurses, Hospital for the Women of Maryland, Baltimore 17, Maryland.

NURSES STUDY CARE DURING DISASTERS

Providing adequate nursing care for the American people in times of disaster is the aim of nursing leaders who met in Washington, D. C., February 20–25, at the first Work Conference on Disaster Nursing sponsored by the American Nurses' Association. The conference was held at Walter Reed Medical Center with Miss Annabelle Petersen, Chairman of the ANA Committee on Nursing in National Defense, presiding.

Miss Helen L. Fisk, Chairman, Maryland State Nurses Association Committee on Nursing in National Defense, attended the conference and spoke on "Maryland Plans for Training Subsidiary Workers." Miss Fisk is Chief of the Division of Public Health Nursing, Maryland State Department of Health, and Chief of the Nursing Unit, Health Services Division for Civil Defense, State of Maryland.

Representatives of nurses associations in the forty-eight states, District of Columbia, Hawaii, Alaska, and Puerto Rico conferred with spokesmen from the military services and public and private health agencies to develop plans to prepare nursing personnel for maximum service during national catastrophies. They also discussed over-all planning and training for disasters useful in local efforts.

Special topics discussed were the role of the nurse in the care of nuclear weapons casualties, community organizations for disasters, adaptations of nursing to disaster needs, what professions are doing to prepare for disaster, and education of the professions for national defense.

ANNOUNCEMENT OF REGULAR CORPS EXAMINATIONS FOR MEDICAL OFFICERS UNITED STATES PUBLIC HEALTH SERVICE

A competitive examination for appointment of Medical Officers to the Regular Corps of the United States Public Health Service will be held in various places throughout the country on June 12, 13, 14, and 15, 1956.

Book Review*

Acknowledgment of all books received will be made in this column, and this will be deemed by us as full compensation to those sending them.

Experimental Tuberculosis—Bacillus and Host. Ciba Foundation Symposium. Little, Brown, and Company, Publishers, Boston. Copyright 1955. 396 pages. $9.00

This book represents deliberations of many world experts in Tuberculosis research. Ciba Foundation made possible a meeting of these experts in London, England 5–7 October 1954. The express purpose was to discuss "The Tubercle Bacillus and the Reactions of the Host Tissues." Dr. Arnold Rich of Johns Hopkins University accepted chairmanship for the meeting. Among the participants from the United States were Drs. Bloch, Hanks, Hirsch, Lurie, Martin, Mayer, Middlebrook, Raffel and Suter; outstanding scientists from England, France, Denmark, Italy, and Switzerland were included in the 38 member group.

Papers were presented on varied subjects with each presentation opened to free discussion and critical comment of all participants. This phase was probably the significant contribution of the meeting. Groups of papers considered the chemistry of the bacillus in relation to its potentialities; mechanism of native and acquired resistance; hypersensitivity and immunity; and included current concepts in relation to drug therapy and cortisone. A final section covered the leprosy bacillus because of its close relationship to the tubercle bacillus. Illustrations are few but of high quality and informative.

This volume is of particular value for research workers in the field of Tuberculosis or Infectious Diseases. Dr. Rich comments that the greatest value of the discussions might possibly be "to clarify the limits of our knowledge of the subjects discussed; for a clearly defined boundary between the known and the unknown is the most stimulating and promising point of departure for the further extension of knowledge." He also points out that "fruitful investigations will result from the cross-fertilization of ideas which has taken place in this very delightful environment.

E. G. B.

*The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

"V-A" CLASSIFICATION NOW BEING USED FOR SOME PHYSICIANS

Colonel Henry C. Stanwood, State Director of Selective Service for Maryland, advises that many physicians and dentists who are special registrants under the so-called "Doctor-Dentist Draft Law" are now receiving a "V-A" classification. This action also includes many special registrants in Priority 4 who were never classified in the past.

The "V-A" classification is being given to those physicians and dentists reaching age 35 who have ever applied for a commission in one of the armed forces in a medical, dental, or allied specialist category and who were rejected for such commission on the sole ground of a physical disqualification.

The "V-A" classification is also being given to all other physicians and dentists upon reaching age 46 unless they are on active duty in the armed forces or are performing civilian work as a Class I-W (Conscientious Objector) registrant.

The "V-A" classification indicates the physician or dentist is over the age of liability for military service under current regulations.

Woman's Auxiliary Medical and Chirurgical Faculty

MRS. ALBERT E. GOLDSTEIN, *Auxiliary Editor*

SEVENTH ANNUAL CONVENTION OF THE WOMAN'S AUXILIARY

The Seventh Annual convention of the Woman's Auxiliary to the Medical and Chirurgical Faculty of the State of Maryland was held at the Sheraton-Belvedere Hotel, Baltimore, May 2, 3 and 4, 1956.

The pre-convention Executive Board met on Tuesday, May 2, 1956, at 9 p.m.

The general session opened at 9:30 a.m., Wednesday, May 2, 1956. Mrs. Gerald LeVan, *president*, presided. Dr. Beverly C. Compton brought greetings from the Faculty and Mrs. John G. Ball responded.

Visiting presidents attended from neighboring state Medical Auxiliaries.

Mrs. Mason G. Lawson, national president, was the honored guest and installed newly elected officers.

The American Medical Education Foundation chairman gave an interesting report on the imperative need of the project and told why it was necessary for every auxiliary member to understand the reasons for a Medical Education Fund.

At noon, the annual luncheon was held in the Ball Room. Doctors and guests attended. The national chairman, Mrs. Lawson was the speaker of the day.

Mrs. LeVan presented the Presidents' pin to Mrs. Homer U. Todd, Sr. and the newly elected president gave her inaugural message. Following the luncheon there was a social hour held in the assembly room from three to five p.m.

The Medical and Chirurgical Faculty Dinner honoring the president, Dr. William H. Warthen, was held on Wednesday evening in the Ball Room of the Sheraton-Belvedere Hotel. Doctors, wives and guests were invited.

The annual Med Chi Ball was held at the Alcazar, Friday, May 4, 1956, at 9 p.m. Dancing, a raffle and other entertaining features made it a very enjoyable evening.

WOMAN'S AUXILIARY
to the
AMERICAN MEDICAL
ASSOCIATION
1956 CONVENTION
CHICAGO: JUNE 11–15
HOTEL CONRAD HILTON

FTC DRAWING UP HEALTH-ACCIDENT INSURANCE CODE

The AMA Washington Letter, No. 84–60

After a trade practices conference in Washington, attended by representatives of state insurance commissions, Blue Cross and commercial insurance companies, the Federal Trade Commission is drawing up a proposed code for the health-accident insurance industry. One of the questions is how closely the FTC code will approach the model state law, drafted and promoted by the Association of State Insurance Commissioners. By March 15 it is expected that the FTC will have suggestions in shape for presentation to the insurance industry. Questions concerned are mostly in the field of advertising and promotion.

WOMAN'S AUXILIARY TO THE WASHINGTON COUNTY MEDICAL SOCIETY

OFFICERS 1956–1957

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Mrs. B. B. Kneisley
148 West Washington Street
Hagerstown, Maryland

President elect and 1st Vice President
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COMING MEETINGS

MATERNAL MORTALITY COMMITTEE

HUNTINGTON WILLIAMS, M.D., *Chairman* IRVIN M. CUSHNER, M.D., *Secretary*

Thursday, June 28, 1956, 4:00 to 5:00 p.m.

Faculty Building, 1211 Cathedral Street, Baltimore

Joint Committee on Maternal Mortality of the Baltimore City Medical Society and the Baltimore City Health Department.

AMA AND BLUE SHIELD CLARIFY POSITIONS ON DEPENDENT CARE

The AMA Washington Letter, No. 84–61

In our LETTERS of January 27, February 3 and February 10 we commented on the hearing conducted by a subcommittee of the House Armed Services Committee on H.R. 7994, a bill designed to provide expanded medical care for dependents of service personnel. We have received questions concerning the manner in which the testimony of certain witnesses was paraphrased by us. The following statements are being published to correct any false impressions which may have been created by our reports:

"In answer to a question covering the type of civilian program recommended by the American Medical Association Mr. C. Joseph Stetler, Director of the AMA Law Department, state that the Association's position was broad enough to encompass either an insurance program or a post-payment mechanism such as the 'home town' medical care program now being used by the Veterans Administration.

"With respect to the testimony presented by representatives for the Blue Shield it should be noted that Dr. Donald Stubbs and Jay C. Ketchum stressed that dependent care could not be accomplished 'through the insurance or medical prepayment plans as they now exist, be they indemnity, service, or a combination of indemnity or service.' They emphasized that the provision of medical care for the dependents of service personnel was an obligation that could 'be discharged fully only by arrangements with the purveyors of the services,' i.e., the medical profession. To illustrate, they indicated that dependent care could be provided in a manner similar to that employed in the so-called 'home town' veteran care program in which the government contracted directly with a medical society for the provision of services. They identified the role of Blue Shield Plans as that of an agent in the administration of this program.

"Dr. Stubbs and Mr. Ketchum emphasized that Blue Shield was 'making no offer for itself' and was not 'proposing that physician care for dependents be provided as a Blue Shield program.' Moreover, they said they were 'convinced that nearly all doctors will support a program in which fees paid in accordance with negotiated schedules will be accepted as payment in full, and that Blue Shield Plans, as the accepted agent of the medical profession in nearly all areas of the United States, can provide the necessary organization and machinery to administer such a program."

AMERICAN MEDICAL EDUCATION FOUNDATION

During July, 1955 the President of the Association of American Medical Colleges sent a questionnaire to all U. S. medical schools to gather information on the cost of undergraduate medical education and the sources of funds supporting the teaching budgets of the medical schools. While there is considerable variation in the accounting systems being used, particularly in the relationship of medical school budgets with teaching hospital, graduate school and research institute budgets, the survey showed the cost of undergraduate medical education per student per year for 1955–56 is approximately $3648.00. Of this amount, the average tuition paid was $682.00. From this it can be seen that tuition pays less than one fifth the cost of undergraduate medical education. The other 4/5 must be obtained from public or private subsidy.

At present costs, by the time the average U. S. student has received his M.D. degree, he has received during his time in medical school a direct subsidy of nearly $12,000.

If the medical student is to continue to receive an education that is in step with the progress being made, there appears to be no possibility to reduce costs.

Doctors perform many services for individuals and for communities, and much of this work is done without compensation. In this way there occurs a balancing of the books in repayment for support given during the educational period.

At the present time, many private medical schools are operating with annual deficits that threaten their existence and many publicly supported schools, because of lack of understanding of medical school costs, receive such low levels of support for their budgets that they are unable to maintain the quality of their teaching programs. It is estimated that the overall deficit in medical education support amounts to approximately $10,000,000 annually.

The National Fund for Medical Education was founded in 1949 under the leadership of President Eisenhower, then head of Columbia University, and other university presidents. This fund is supported by the American Medical Association, The Association of American Medical Colleges and the National Association of Manufacturers. From 1951 to date about 9½ million dollars have been raised and distributed to medical schools. While this amount has been inadequate to cover the deficits, it has been of great assistance in maintaining progress in medical education. Conference with industry has established the belief that if the doctors can raise approximately 2 million dollars annually, industry can raise 8 million dollars. It therefore seems possible to reach the goal of solving the medical school deficits.

During 1955, 260 doctors in Maryland contributed $4,692.00 to the American Medical Education Foundation. Over 2500 doctors are in active practice in Maryland and if the gifts made last year were prorated, it would only represent approximately $1.90 each. Because only a little over 10% of the doctors contributed, this record is so poor that major industries are considering cancelling their annual contributions because they feel that they should not be expected to support medical education if physicians themselves have so little faith in its needs.

An annual contribution of $10.00 per physician in the U. S. would raise the $2,000,000 set as the goal for physicians, and if raised would be a challenge for industry to match it with 8 million. It is hoped that many will find it possible to contribute more than the minimal goal, and that none will forget the assistance they received in medical school so that succeeding classes in medicine may have the same opportunity. Funds contributed can be earmarked by the donor and will be given to the medical school so designated.

Help your medical school by contributing annually to the American Medical Education Foundation.

A check mailed now helps to insure progress in medical education.